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Comparing the efficacy of group and individual psychological therapy for persistent depression and evaluating effectiveness and change processes in group Cognitive Behavioural Analysis System of Psychotherapy for persistent depression in an outpatient setting.

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Submitted in part fulfilment of the Doctorate in Clinical Psychology

The University of Edinburgh

2021

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Acknowledgements

Firstly, I would like to thank my supervisors, Dr Tim Bird and Dr Massimo Tarsia for making this thesis possible. Their combined support, expertise, encouragement and faith in me has been invaluable.

To Stewart Buchan for all the hard work on the CBASP groups.

Thank you to Tom Todd, expert by experience, who kindly gave input on my original thesis which could not progress due to the COVID-19 pandemic.

Thank you to my cohort of trainees who have been supportive over the years, especially Alex, Nienke and Miriam.

Most of all thank you to Paul, for the love, support and belief in me through the years of study and to Euan and Alice who have encouraged and kept me smiling even when things were not easy. Also, thank you to my family and friends for the never-ending emotional and practical support.

Finally a huge thank you to all the participants, who without their input this research would not have been possible.

Thesis Abstract

Background. Persistent depression (PDD) is a difficult to treat condition with poor outcomes. There is a growing evidence base for psychological treatment for PDD and it is recommended there is an interpersonal element to therapy. However, much is still to be discovered about the relevant moderating and mediating variables involved in successful treatment. Group psychotherapy is thought to be as effective as individual therapy for Major Depressive Disorder but little is known about any possible advantages in treating PDD. Cognitive Analysis System of Psychotherapy (CBASP) was developed by McCullough (2000) to specifically treat PDD and involves a cognitive, behavioural, psychodynamic and interpersonal approach. Research has shown it to be effective at reducing depression symptoms and increasing interpersonal functioning in both individual and group formats. Interpersonal learning acquisition is measured in CBASP and it is theorised that this precedes symptom improvement as a person learns to apply the skills out-with the therapy room.

Purpose. A systematic review and meta-analysis sought to compare group and individual psychological therapy to establish if there was any advantage to group therapy in individuals with PDD. An empirical study reviewed the outcome data from 13 groups of CBASP (CBASP-G) which was delivered in an outpatient setting to examine the process of change.

Methods. A systematic review of the literature identified randomised controlled trials (RCT) that used psychological therapy for PDD. Twenty studies met the inclusion criteria, and a meta-analysis was performed to compare the effectiveness of group and individual therapy using post mean effect sizes. Studies were checked for risk of bias. Subgroup analyses were used to investigate the impact of moderators such as control type (active or inactive) and depression type (chronic depression or dysthymia). Outcome data from CBASP-G was gathered for the empirical study and extracted and analysed

using paired t-tests and multilevel modelling statistical methods. Overall effectiveness, pattern of change of symptoms (overall distress and mood), skill acquisition, interpersonal functioning and global measures of improvement were examined in the analysis.

Results. Group psychotherapy was found to have a moderate significant effect compared with a small effect for individual therapy, and the subgroups were significantly different. However, the sample had substantial heterogeneity and moderator analyses found that type of depression, control, and risk of bias were important factors when considering the results. In the empirical study CBASP-G was found to significantly improve depression, distress and mood symptoms. Significant change was found in the hostile-submissive interpersonal domain. Multilevel modelling revealed that skill acquisition improved the model fit significantly, but not all types had a significant result. Change was found to be linear for symptoms and quadratic for skill acquisition.

Discussion. The thesis findings give preliminary evidence that psychological treatment for PDD is effective and that there may be an advantage to group delivery. Additionally, it gives some support to McCullough's (2000) model that CBASP-G is an effective treatment for PDD, and skill acquisition is important in facilitating interpersonal change and symptom improvement. The review indicates that higher quality studies and further research are required to examine the impact of variables and moderators that are likely to have an impact on any differences between group and individual treatment. Longer follow up would help investigate the role of skill acquisition and routine analysis of the current provision of treatment for PDD in community settings is recommended.

Lay Summary

Introduction. Depression is the biggest cause of disability worldwide. Around a third of people that suffer from depression have it long term. This type of depression can be hard to treat and is called persistent depression (PDD). There is growing evidence that psychotherapy can treat PDD, but little is known about the factors that make treatment effective. Group therapy offers an opportunity for interpersonal learning which has been shown to be important in treating people with PDD. Cognitive Analysis System of Psychotherapy (CBASP) is specifically designed to treat PDD, and it can be delivered in an individual or group format. This therapy helps the person to learn how their interactions in relationships can be unhelpful and it encourages them to try a different approach which can help them have better results and make them feel better.

Aims and methods. The first part of this thesis combines research studies for PDD that use individual and group formats to see if there is any difference in efficacy. The second part of the research is to find out if learning the skills in a group version of CBASP (CBASP-G) makes people feel less depressed and distressed. Data from 80 people who attended a group at an outpatient clinic was examined to look at the patterns of change in symptoms. A statistical method called multilevel modelling was used to do this, by applying different models to the data to see what factors were important. Understanding the process of change during therapies helps to make treatment better for those that need it.

Main findings. Group psychological therapy was found to be more effective than individual therapy, but the difference could be due to a number of factors. These include the type of depression, type of therapy and control used. CBASP-G was effective at reducing depression and distress symptoms. The learning in CBASP-G appeared to be important for the reduction in symptoms

but longer follow and more high-quality research will be required to improve treatment for people with persistent depression.

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Comparing the efficacy of group and individual psychological therapy for persistent depression.

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[1] Written in accordance with guidelines for Clinical Psychology Review

Chapter 1 Meta-analysis

1.1 Abstract

Background. Persistent depressive disorder (PDD) is a debilitating condition which puts a heavy burden on mental health services. PDD is more difficult to treat than episodic depression and has poorer outcomes from treatment. Individuals with PDD typically have impoverished interpersonal functioning, and it is theorised this is linked to experiences of childhood maltreatment. Group psychotherapy has some advantages compared to individual therapy including being cost effective and allowing more people to be treated per therapist. Meta-analyses have found evidence that individual and group therapy for depression are similar in efficacy. Research points to there being an additional interpersonal benefit for group therapy. Little is known about any differences in effect of group or individual treatment for PDD. This exploratory meta-analysis was designed survey the literature to compare the effect of group versus individual psychological therapy for PDD and consider the effect of possible moderators.

Methods. A systematic search of the literature was completed to source randomised controlled trials (RCT) of psychotherapy for PDD. Twenty studies met the criteria for inclusion. Studies were assessed for risk of bias using the RoB2 software and inter-rater reliability tested for the sample. Data was extracted from the 20 studies with post therapy mean effect sizes used to compare psychotherapy for PDD versus a control. A meta-analysis was carried out to compare group versus individual treatment for PDD. Subgroup analyses were carried out to examine the impact of type of control (inactive or active), type of PDD (chronic depression or dysthymia), and risk of bias.

Results. There was a significant difference found in favour of group treatment in the 20 studies found. A small mean effect size was found for individual

therapy (14 studies with 31 different arms) *d*= 0.27 (95% CI: -0.42, -0.11), *Z*=3.34, (*p*<0.001), and heterogeneity was I^2=77% (p<0.001) compared with a moderate mean effect size for group delivery (6 studies with 13 different arms) *d*=-0.53 (95% CI: -0.80, -0.26) *Z*= 3.83 (p<0.001) and heterogeneity of I^2=60% (p<0.01). Testing for subgroup differences highlighted there was a significant difference between individual and group therapy using the *p*-value of 0.10 to assess for heterogeneity (I^2 = 63.3%, *p*=0.10). Analysis for publication bias found no concerns. Most studies had an element of risk of bias. Further moderator analyses explored the impact of outliers, type of depression and control type (active or inactive).

Conclusions. Group therapy for PDD demonstrated an advantage over individual therapy. There were many confounding variables which affected this analysis and their impact is unclear. Type of control, type of depression and quality of study were all likely confounding factors. The type of therapy and dose of sessions were not accounted for but likely important in their impact. Limitations and suggestions for future research are discussed.

Keywords. Persistent depressive disorder (PDD), Chronic depression, Dysthymia, Psychotherapy, Psychological therapy, Group therapy, Individual therapy, Meta-analysis.

1.2 Introduction

Caspi & Moffitt (2020) found that the majority of people will experience a mental health disorder in their life, but most will have more than one and a variety of issues, therefore, mental health problems should be expected. The impact of early onset disorders on the increase of number and variety of mental health problems means that early intervention and prevention is important. Depression is a global concern, with persistent depressive disorder (PDD) having worse outcomes and a poorer response to treatment than other types of depression (Jobst, et al., 2015; World Health Organisation (WHO), 2020). This paper will review the current evidence base for treatment of PDD and look at different types of delivery by individual or group therapy modes. The aim of the study is to systematically review randomised controlled trials (RCT's) of psychological treatments for persistent depression and perform a meta-analysis to investigate if there are any benefits from group treatment compared to individual treatment. The results are presented and future directions for research are suggested.

1.2.1 Depression impact prevalence and factors

Depression is one of the most frequently occurring mental health problems and is estimated to affect around 6.9% of the population (Wittchen et al., 2011) or 264 million people globally (Sheikh et al., 2018) making it a global priority (WHO, 2020). Prevalence has been rising in the UK since the start of the COVID-19 pandemic, with up over 20% of UK adults reporting symptoms of depression in the first half of 2021 (Office for National Statistics (ONS), 2021). The burden of depression is extensive, with it being one of the biggest contributors to disability worldwide (Wittchen et al., 2011).

1.2.2 Persistent/chronic depression and dysthymia

Around a fifth to a third of people with depression are thought to have a chronic course, lasting over two years and from around a third to a half of people utilising specialist mental health services are estimated to have PDD symptomology (Arnow & Constantino, 2003; Klein & Santiago, 2003; Rubio et al., 2011; Torpey & Klein, 2008). PDD differs from episodic depression in that the depressive symptoms should be present for at least 2 years with less than 8 weeks remission. It can be characterised as either early or late onset (before/after age 21) (American Psychiatric Association (APA), 2013). Chronic depression was the term commonly used for this type of depression until it was recently re-classified as PDD in the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) (American Psychiatric Association, 2013). PDD is classified as either dysthymia (persistent mild depression), chronic depression, double depression (Major Depressive Disorder (MDD) with dysthymia), and recurrent MDD with incomplete recovery between episodes (Schramm et al, 2008). International Classification of Diseases 11th revision (ICD-11) use a coding system to define the persistent element of MDD and use similar definitions of 2 years without remission (World Health Organization, 2018). Research has suggested that dysthymia is similar to chronic depression, or indeed, part of the same disorder leading to it being combined into PDD (American Psychiatric Association, 2013; Klein & Santiago, 2003; Torpey & Klein, 2008). However, there is some dispute over the validity of the concept of dysthymia as research has showed there is significant overlap with MDD and anxiety disorders with the suggestion that dysthymia combines PDD with an anxiety disorder, and links this to neurotic personality traits (Hidalgo et al., 2012; Klein et al., 2000; Rhebergen & Graham, 2014). Treatment-resistant depression (TRD) differs from PDD and is generally defined as not responding to two doses of antidepressant medications of an “adequate” dose and duration (Fava, 2003). PDD and TRD can be loosely defined in studies and while they are similar concepts a patient may fit one of the definitions or both. The pooling of TRD and PDD can be problematic as the concepts are different

and therefore treatment effects could be different (Cuijpers et al., 2020, Jobst et al., 2015).

People experiencing PDD are more likely to have social and economic impairments, earlier age of onset, lower self-esteem, poor overall health, more likely to have suicide attempts, higher healthcare usage, more co-morbid health conditions and less likely to respond to anti-depressant medication compared to non-chronic courses of depression (Jobst, et al., 2015; Köhler et al., 2019; Rubio et al., 2011; Schramm et al., 2006). The same is roundly true for those with a diagnosis of dysthymia with most eventually developing major depression episodes during their lifetime (Klein et al., 2000). Indeed, the individual, family and societal impact is widespread with higher co-morbidities of other mental health and medical problems than those with non-chronic depression (Köhler et al., 2019; Murphy & Byrne, 2012).

There are various factors that have been implicated in the development of PDD including childhood maltreatment (neglect, emotional/sexual/physical abuse), (Cicchetti & Barnett, 1991, Lizardi et al., 1995; Wiersma et al., 2009). However, the evidence for the impact of childhood maltreatment is mixed with a recent review finding the link inconclusive (Köhler et al., 2019). Deficits in interpersonal functioning has been found to be more prevalent in persistent forms of depression and studies have found this factor is important in how PDD is maintained (Leader & Klein, 1996). Bird et al. (2018) and Köhler et al. (2019) found that socially avoidant styles were linked to PDD rather than episodic depression and this finding builds on previous research that decreases in hostile-submissive traits improved depression symptoms (Constantino et al., 2008; Constantino et al., 2012).

1.2.3 Treatment for PDD

Treatment rates for mental health problems are low with Wittchen et al. (2011) finding that less than a third of people in Europe received support for their mental health condition. Worldwide it is estimated in lower income countries that only 15-24% receive any treatment for depression (Wang et al., 2007). Reduced social support is a predisposing factor for depression which can interfere with a person's ability to navigate treatment and could make them more likely to drop out of treatment (Keller et al., 2014). Treatment resistance has been linked with higher suicide risk, co-morbid anxiety, more hospitalisations, childhood maltreatment, higher doses of anti-depressants and longer depressive episodes (DeCarlo et al., 2016; Nanni et al., 2012). Arnow & Constantino (2003) argue that long term treatment is required to ensure full recovery and prevent relapse and they highlight that work and social functioning may take longer to improve than depressive symptoms alone.

1.2.3.1 Types of interventions

1.2.3.1.1 Medication

Anti-depressant medication is a recommended treatment for PDD and its use is steadily increasing (Kendrick et al., 2021). More than 10% of adults in England were prescribed anti-depressants (for varying reasons) in March 2018 alone (NHS Digital, 2019). However, there are issues with relying on medication for treatment with the rates of remission for PDD patients being less than 30% (Ijaz et al., 2018; Krystal et al., 2011; Trivedi et al., 2006). It is possible the true rates of remission are even lower since the RCT trials that provide the evidence lack ecological validity, such as excluding participants with co-morbid disorders, which are extremely prevalent in PDD (Trivedi et al., 2006). Also, withdrawal and side effects from anti-depressants, (such as problems with sleep, weight gain and sexual dysfunction), are common, can be severe, and can be mistaken with depression symptoms in measures such as the HDRS-17 and BDI-II (Hieronymus et al., 2021; Kendrick et al., 2021; Saha et al., 2021).

1.2.3.1.2 Psychological therapy

Psychological therapy is often a preferred treatment method and recommended psychological interventions for treating persistent depression include CBT, Inter-personal psychotherapy (IPT), behavioural activation, and Cognitive Behavioural Analysis System of Psychotherapy (CBASP). (The Matrix, 2015; McHugh et al., 2013; National Institute for Clinical Excellence (NICE), 2009). The evidence base for treating PDD with psychotherapy has been demonstrated in previous meta-analyses (Cuijpers et al., 2010; Furukawa et al., 2018). Cuijpers et al. (2010) first combined the RCT data on chronic depression and dysthymia in a meta-analysis compared by type of control (inactive, active, combined treatment). They found a significant small effect for psychotherapy compared with inactive controls, but psychotherapy was less effective than pharmacotherapy. However, the studies that brought down the effect size were dysthymia treatment studies indicating that either that dysthymia was less receptive to the psychotherapy offered or more responsive to medication (Cuijpers et al. 2010).

It is important to note that there are issues with operationalising RCT's into real world settings (Schindler et al., 2011). Indeed, Riihimaki et al. (2017) found that only half of depressed primary care patients who needed maintenance treatment received it, and then for less time that was recommended, thus putting the patient at increased risk for relapse and decreasing the impact of treatment. Research suggests the dose of treatment is important for PDD and that intensive but also prolonged treatment is warranted, with Cuijpers et al. (2010) suggesting 18 sessions were a minimum amount (Dunner, 2001; Schramm et al., 2019). This is an important feature as Schramm et al. (2015) highlighted that certain interpersonal behaviours such as being extremely passive, or aggressive are not explicitly dealt with in some types of therapy like IPT while the CBASP manual directly addresses this point.

1.2.3.1.3 Combined treatment

Evidence points to combination treatment of psychotherapy and medication being the most effective and desirable treatment (Arnow & Constantino, 2003) and the European Psychiatric Association recommend combined treatment with an interpersonal element (Jobst et al., 2015). Cuijpers et al. (2020) demonstrated that combined treatment is most effective for chronic and treatment resistant depression with recommendations that if only one mode of treatment is available then psychotherapy should be offered over medication. Unfortunately, this is not the case routinely with many people not getting any suitable treatment for PDD (Koscis et al., 2008). Guidi et al. (2020) suggest a sequential approach to reduce recurrence of depression is to integrate psychotherapy after acute phase medication and this can be alongside continued medication. They highlight the importance of increased psychological well-being while removing residual symptoms as being key to this. Cuijpers et al. (2020) found that acceptability of treatment (defined as drop out for any reason) was highest in combined treatment, then psychotherapy alone was more acceptable than medication alone. This may be due to increased risk of side effects in medication and patient preference leaning towards psychotherapy rather than medication treatment (McHugh et al., 2013). Long term follow up also shows that for depression combined treatment is more effective than medication alone and psychotherapy more effective than medication (Cuijpers et al., 2020; Cuijpers et al., 2013), however, there is a paucity of long term follow up studies and more data is required to investigate this. Research points to combined treatment effect being independent parts of both treatments rather than a true combined effect (Cuijpers et al., 2014).

1.2.3.2 Group treatments

Group psychotherapy originates from when a physician treating a few individuals how to manage tuberculosis, observed spontaneous peer support occurring in the sessions (Freedheim, et al., 1992). Indeed, there appear to be many advantages of group delivery of psychotherapy including reduced costs

and therapist time and being able to treat more people at once (Morrison, 2001; Tucker & Oei, 2007). Group CBT for depression has been found to be cost effective compared with individualised therapy but there is a lack of high-quality studies using comprehensive costing models to give a definitive answer on the scale of the cost effectiveness, and for some conditions (e.g. alcohol and substance misuse) individualised therapy may be more cost effective (Tucker & Oei, 2007). Fogarty, et al., (2019) found group CBT was not only economical and effective at reducing symptoms of social anxiety and depression but that the symptom improvement was sustained over the long-term indicating the participants developed skills of becoming their own "therapist". Additional benefits have been cited in the literature and include improved interpersonal functioning, a positive impact of a cohesive group, peer modelling, and participants obtaining a shared understanding of the difficulties they are experiencing (Lewinsohn & Clarke, 1999; Morrison, 2001). In a more recent study on young people who had experienced domestic violence the group format enabled a gradual feeling of safety within the group which was thought to allow the process of accepting and giving of support to others. Furthermore, a strength of this format was thought to be the enhanced opportunity to talk through how their complex family relationships had affected them (Fellin, et al., 2019). Yalom & Leszcz (2005) highlight that this giving and receiving support cultivates a stronger, therapeutic alliance than one would see in individual therapy and the identification with others in the group fuels sharing and insight into one's own issues. This process is thought to allow the development of social and communication skills and even support individuals to be able to receive criticism (Yalom & Leszcz, 2005).

However, there are some disadvantages including the reduced ability to personalise the treatment to the individual's needs, risks of a person dominating the sessions or subgroups forming which could interfere with the group's overall progress, (Morrison, 2001; Tucker & Oei, 2007). Furthermore,

the group environment may make it harder for some to disclose personal thoughts that might help with progress in therapy (Morrison, 2001).

Cuijpers et al. (2019) network meta-analysis on CBT for depression found 81 of 101 studies were delivered in individual format, despite evidence that psychotherapy is also effective across group, internet or guided self-help delivery models. There were no significant differences between acceptability of different methods of CBT treatment when comparing individual, group, and telephone CBT, though, guided self-help was less preferred than individual therapy (Cuijpers et al., 2019). Cuijpers et al. (2020) recommend that alternative modes of treatment such as group therapy should be used in routine practice.

Group treatment such as CBASP for PDD has been shown to reduce depression symptoms and increase interpersonal functioning (Sayegh et al., 2012; Locke et al., 2017). Locke et al. (2017) noted the fear their group participants had at evoking anger or scorn from others, and this made it difficult for them to assert themselves at the start of therapy, though this changed as the group treatment progressed. This points to there being an added benefit to group delivery in practicing difficult social circumstances with others who have similar problems, and that the group environment can offer a conducive, safe atmosphere to do this (Sayegh et al., 2012). However, there appears to be a lack of research on comparisons of different delivery modes of therapy for PDD.

1.2.4 Rationale for meta-analysis

As depression rates are rising, partly due to the impact of COVID-19 pandemic (ONS, 2021), and with PDD patients using disproportionately more mental health services, cost and time effective solutions are vital to meet this burden

(Torpey & Klein, 2008). Group therapy is effective at treating many mental health problems, has advantages in being more cost effective, with a potential peer interaction benefit and has been shown to be effective for PDD (Locke et al., 2016; Morrison, 2001; Sayegh et al., 2012; Tucker & Oei, 2007). Additionally, no significant difference was found between individual and group CBT therapies for non-chronic types of depression (Cuijpers et al., 2019). PDD is difficult to treat and there may be added advantages to the group set up that benefits those with PDD who likely have interpersonal difficulties (Jobst et al., 2015; Pettit et al., 2008). Therefore, this study aimed to explore this topic by systematically reviewing the literature for RCT's that treat PDD and comparing the effectiveness between group and individual modalities through a meta-analysis. The impact of moderators such as control type or depression type were examined. It was hypothesised that psychotherapy for PDD would be effective, and that group treatment could show an advantage over individual treatments.

1.3 Methods

1.3.1 Identification and selection of studies

1.3.1.1 Inclusion criteria

Studies in English which included RCT's of psychotherapy for persistent/chronic depression. The DSM-5 criteria for persistent depression was used with studies meeting the criteria for one of the following:

- Chronic/persistent depression
- double depression (MDD with dysthymic disorder) or
- recurrent depression with incomplete remission between episodes
- dysthymia

all lasting for 2 years or longer. No age limit was selected. Psychotherapy was defined as psychologically informed intervention.

The term “chronic depression” (DSM-IV) is used to combine chronic/persistent depression, double depression and recurrent depression with incomplete remission between episodes and separate from dysthymia. These terms “chronic depression” and “dysthymia” are used in the analysis below.

1.3.1.2 Exclusion criteria

Studies which were not available in English or did not have post mean data available were excluded. Studies where the participants did not meet the PDD criteria were also excluded.

1.3.1.3 Literature search strategy

A literature search was carried out using the following databases and date range: APA Psych articles full text (to 4th December, 2020), Embase Classic and Embase (1947 to 4th December, 2020), Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily (1946 to 4th December, 2020), and PsycInfo (1806 to 4th December, 2020).

The search was carried out in each database using the following search terms: (("chronic* depress*" or "persist* depress*" or "treat* resist* depress*") OR ("chronic MDD" or "chronic major depress* disorder" or "recurrent MDD" or "recurrent major depress* disorder" or "dysthymi*") OR (“depress*neurosis” or “refractory depress*” or “treatment resist* depress*”). AND ("therap*" or "inter*" or "psycho*therap*"). AND ("random*" or "rct") ab,ti. The analysis was registered on Open Science Framework (OSF) (osf.io/72fa8).

The search terms were tested to pick up known papers from other meta-analyses (e.g., Cuijpers et al., 2010, Cuijpers database Open Science Framework (OSF), 2019) and terms adjusted and added to fit (e.g., depressive neurosis and treatment resistant depression). Papers that met the inclusion criteria were searched for references of other studies and hand search completed of papers referring to chronic/persistent depression. Articles that were identified by search were screened and duplicates were removed (Figure 1.) in accordance with PRISMA guidelines (Moher et al., 2009). Articles identified from other papers and that had been screened were compared with the inclusion/exclusion criteria. Those that met the criteria were included in the meta-analyses. Articles that were less clear about meeting inclusion criteria were checked with author[a] and a consensus was reached about inclusion.

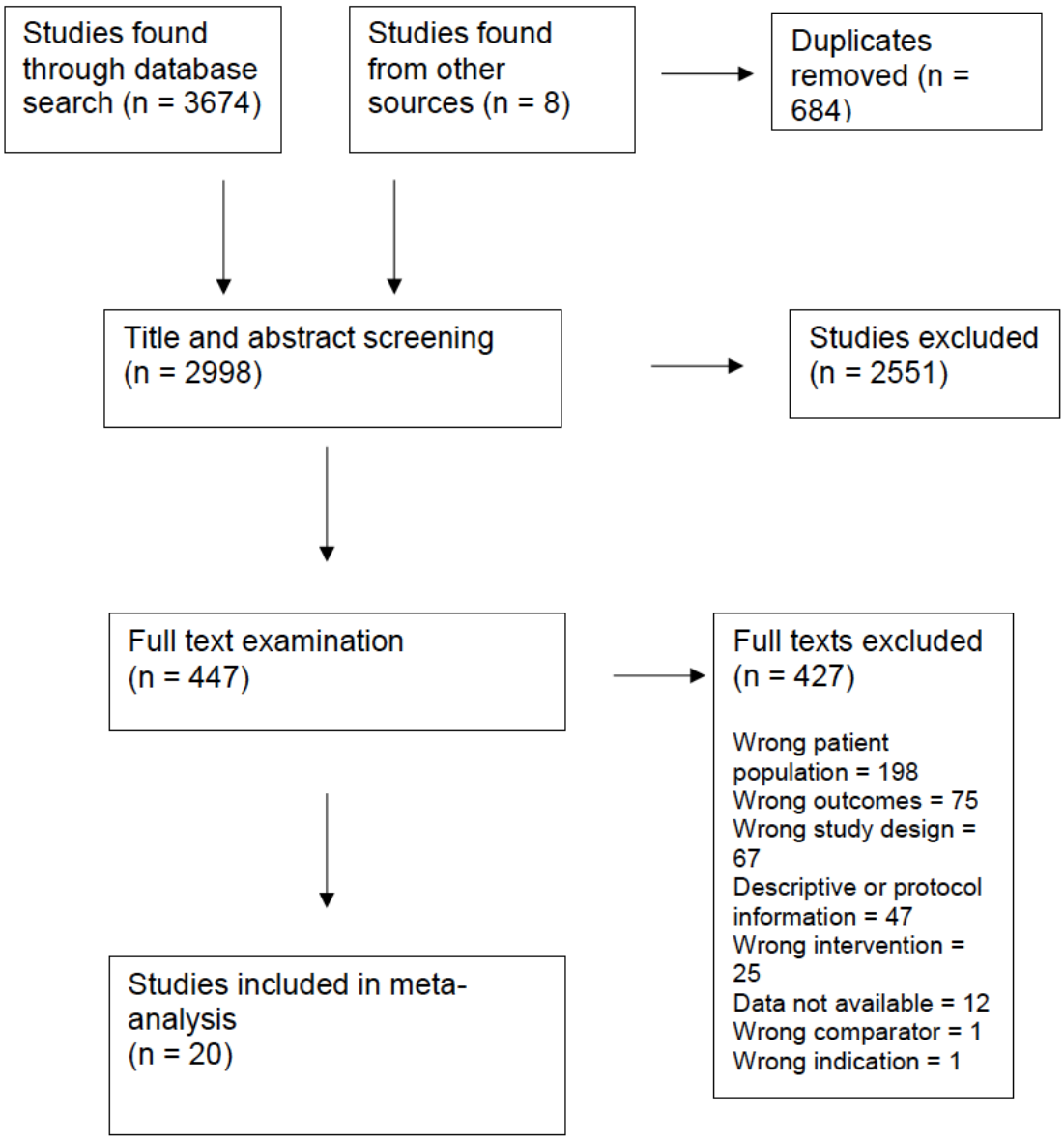


Figure 1. PRISMA flow diagram (Moher et al., 2009).

1.3.2 Risk of bias assessment

The studies were assessed using the Cochrane revised risk of bias tool for randomized trials (RoB 2) (Sterne et al., 2019). This checked the validity of the studies for the following criteria: Randomisation process; Deviations from the intended interventions; Missing outcome data; Measurement of outcome; Selection of the reported result. Each study was ranked for each criterion as

either Low risk, Some concerns, or High risk. Each study was then given an overall risk Low risk, Some concerns or High risk. This allowed for the studies to be rated accordingly for areas that are likely to produce bias (Higgins et al., 2016).

1.3.3 Meta-analyses and data extraction

Data extraction was carried out by the first author, and a sample checked by the second author. Any discrepancies or studies that were unclear were discussed and agreed upon between authors. The effect size of difference between the psychotherapy intervention and the control (active or inactive) was calculated at post-test for each comparison using Cohen's *d* standardised mean difference, since outcome measures were not all the same (Higgins et al., 2019). This was taken from the end of therapy depression score means and standard deviations. Few studies reported follow up data, so a decision was made to look at end of therapy alone. Size of effect was considered as follows: 0.2 = small; 0.5 = moderate; 0.8 = large (Cohen, 1988). Cuijpers et al. (2014) has suggested that a clinically meaningful cut off could be 0.24. Measures of symptoms of depression were used and if two outcomes were reported the independently assessed (non-self-report) one was used. The depression measure post mean was extracted with standard deviations (SD) for each intervention and control; in some studies, there were multiple arms for comparison. In studies with insufficient reporting of data, attempts were made to contact the authors and if the post-mean values could not be sourced the study was excluded from the meta-analysis.

A series of meta-analyses were conducted utilising Review Manager (RevMan) 5 (2020) software to calculate the pooled mean effect sizes (standardised mean difference) from the post means and SDs (Higgins et al., 2019). Since, significant heterogeneity was assumed likely due to errors within and between studies, and that the studies have variations in average effect

size, a random effects model was used (Field, 2005a). The level of statistical significance was set at $p< 0.05$. Where combination of psychotherapy and medication was being compared to other therapy this was input with the experimental condition being the combination therapy. Similarly, when two therapies were being compared the experimental condition was compared with the other therapy as control. Analysis was performed by separating active controls (other therapy, medication) and inactive controls (waiting list, TAU, CAU, placebo). Some of the studies had multiple arms which duplicates the participant data and may artificially affect the heterogeneity or the effect size of the meta-analysis. A decision was taken to follow the procedure used by Cuijpers et al., (2010) and Cuijpers et al., (2011) in their meta-analyses looking at chronic depression and Interpersonal Psychotherapy for depression, of using multiple arms rather than combining arms, since the effect of the type of control was of interest to this study. Cuijpers et al., (2010 & 2011) carried out additional meta-analyses to look for any effects of using the multiple arms using one sample of the data for largest effect size and for smaller effect size. Likewise, an additional analysis was carried out using one sample of each participant group of data from each study - one carried out using the largest effect size and one using the lowest effect size. This did not significantly change the effect size of the overall result or reduce the heterogeneity which was still classed as high (Table 2.).

The chi-squared test and I^2 statistic was calculated to categorise the impact of heterogeneity in percentage on the ES estimates using the following levels of heterogeneity: 0 to 40% might not be important; 30-60% possible moderate; 50-90% possible substantial; 75-100% possible considerable high. Caution is advised in using the chi-squared test alone due to lack of power and small sample sizes typical in meta-analyses and using the p-value of 0.1 is suggested rather than 0.05 to assess heterogeneity. (Higgins et al., 2003; Deeks et al., 2021). Sensitivity analyses was performed in each subtest to investigate the impact of possible outliers. Outliers were defined if the 95% CI

lay out with the mean pooled effect size for the meta-analysis. Subgroup analyses were calculated where possible to examine the impact of depression type (chronic depression or dysthymia) and control type (active or inactive).

1.3.3.1 Other analyses

Publication bias was evaluated by inspecting the funnel plot from the comparisons and performing a regression test for asymmetry of the funnel plot (Egger, 1997), file drawer analysis (Rosenthal (1995) approach), Duval & Tweedie (2000) trim and fill procedure, and a weight function model for publication bias (Vevea & Hedges, 1995). Inter-rater reliability was assessed for the risk of bias scoring. Supplementary analysis was completed using Shiny app for R (MAVIS; Hamilton & Mizumoto, 2017). The Cochrane Review Guidelines (Higgins et al., 2019) formula for pooling means were used (Figure 2).

	Group 1 (e.g. males)	Group 2 (e.g. females)	Combined groups
Sample size	N_1	N_2	$N_1 + N_2$
Mean	M_1	M_2	$\frac{N_1M_1 + N_2M_2}{N_1 + N_2}$
SD	SD_1	SD_2	$\sqrt{\frac{(N_1 - 1)SD_1^2 + (N_2 - 1)SD_2^2 + \frac{N_1N_2}{N_1 + N_2}(M_1^2 + M_2^2 - 2M_1M_2)}{N_1 + N_2 - 1}}$

Figure 2. Formula for combining means (SD's) into one group (Higgins et al., 2019).

1.4 Results

A total of 3682 studies were found by the database and hand search. 684 duplicates were removed. A total of 2551 studies were eliminated during the

abstract and title screening stage leaving 447 studies were subject to a full text examination. Twelve studies were rejected as they did not have the appropriate data available. Some of these authors were contacted (if the paper was within the last five years) but no extra data was provided by them. A total of 20 studies met the inclusion criteria and were used in the meta-analysis. Most studies were carried out in the Europe, US or Canada, with two studies out with this (Ebrahimi et al., 2013 (Iran), de Mello et al., 2001 (Brazil).

All studies used validated depression measures with most studies using the clinician rated Hamilton (1960) depression scale (HRSD/HAM-D) and only four the studies using other measures (BDI-II (Ebrahimi et al., 2013, Strauss et al., 2012) – two, MADRS (Browne et al., 2002) – one and IDS (Wiersma et al., 2014) – one).

1.4.1 Characteristics of included studies

Within the 20 studies there was data from 2538 participants, of those 1708 received a form of psychological therapy. Interventions included combinations of CBT (6 studies), CBASP (6 studies), IPT (7 studies), with utilisation of CBT based interventions BPT, MBCT, SIPT, psychodynamic therapy, LTPP, and non-specific control therapy BSP and SP (4 studies). Controls included combinations of active controls (medication (9 studies), other therapy (10)), and inactive controls (wait list (4), placebo (2), TAU or CAU (4)). The characteristics of the sample are shown in Table 1. The mean participants per study was 126.9. The number of sessions of therapy planned ranged from 8 to 60 sessions with a mean (SD) of 19.3 (-12.5).

Table 1. Description of included studies

Author Year	Intervention	N	Sex (% female)	Age (Years)	Planned (sessions)	Country	Recruited	Type of Depression	Depression Measure	Group or Individual	Treatment quality
Agosti (1997)	CBT	16	NR	31.3 (6.4)	16	US	Clinical	Chronic depression DSM III-R	HDRS	Individual	M/Mo/T
	IPT	14			16						
	Imipramine	20									
	Placebo	15									
Browne (2002)	IPT	83	68%	42.1 (12.0)	12	Canada	Primary care	DYS DSM-IV MDD 15%	MADRS	Individual	Mo/T
	IPT/Sertraline	122			12						
	Sertraline	117									
De Jong (1986)	CBT	10	70	36.6 (7.5)	37	Germany	Inpatient	MDD and DYS DSM III	HRSD	Individual and CBT arm had group element	Mo/T
	CT	10			50						
	W/L	10									
Dunner (1996)	CT	11	45.8	35.7	16	US	NR	DYS DSM-III	HRSD	Individual	M/Mo/T
	Fluoxetine	13									
Ebrahimi (2013)	SIPT	16	55	31.81 (10.31)	8	Iran		DYS DSM-IV	BDI-II	Individual	M
	CBT	16		31.25 (8.82)	8						
	W/L	15		29.06 (9.5)							
	Medication	15		32.26 (10.36)							

Author Year	Intervention	N	Sex (% female)	Age (Years)	Planned (sessions)	Country	Recruited	Type of Depression	Depression Measure	Group or Individual	Treatment quality
de Mello (2001)	IPT/moclobimide	11	80	NR	16	Brazil	Outpatients	DYS or DYS+MDD (91%) DSM-IV	HAM-D	Individual	T
	Moclobemide/TAU	13									
Fonagy (2015)	LTPP/TAU	67	66.7	42.7 (10.4)	60	UK	Primary care	MDD + 2 years current episode (DSM-IV)	HRSD	Individual	M/Mo/T
	TAU	62	66.1	46.1 (9.9)							
Harpin (1982)	CBT	6	41.7%	42.0	20	UK	Clinical	Chronic over 2 years	HAM-D	Individual	T
	W/L	6									
Keller (2000)	CBASP	216	65.3	43 (10.7)	16	US	Outpatients	Chronic DSM-IV	HRSD	Individual	M/Mo/T
	CBASP/nefazadone	226			16						
	nefazadone	220									
Koscis (2009)	CBASP/medication	174	56	45.3 (11.9)	16	US	Clinical	Chronic DSM-IV	HAM-D	Individual	M/Mo/T
	BSP/medication	168	57.9	46.4 (11.7)	16						
	Medication	76	49	43.2 (13.4)							
Markovitz (2005)	IPT	23	63	42.3 (12.3)	16	US	Community	Early-onset DYS DSM-IV	HAM-D	Individual	M/Mo/T
	IPT/sertraline	21			16						
	sertraline	24									
	BSP	26			16						

Author Year	Intervention	N	Sex (% female)	Age (Years)	Planned (sessions)	Country	Recruited	Type of Depression	Depression Measure	Group or Individual	Treatment quality
Markovitz (2008)	IPT	14	31%	38.4	16	US	Community	Early onset DYS (SCID)	HAM-D	Individual	M/Mo/T
	BSP	12			16			MDD (54%)			
Michalak (2015)	CBASP/TAU	35	62.9	50.2 (10.5)	8	Germany	Community	Chronic DSM-IV	HAM-D	Group	M/Mo/T
	MBCT/TAU	36	58.3	48.4 (11.5)	8						
	TAU	35	65.7	54.0 (13.24)							
Ravindran (2000)	CBT/sertraline	25	57.7	NR	12	Canada	Community	DYS DSM-IIIR or DSM-IV	HAM-D	Group	T
	CBT/Placebo	24			12						
	Sertraline	22									
	Placebo	26									
Rohricht (2013)	BPT	11	41.9	46.9 (11.7)	20	UK	Outpatients	Chronic DSM-IV	HAM-D	Group	M/Mo/T
	W/L	12		48.5 (9.1)							
Schramm (2017)	CBASP	124	66	44.9 (11.8)	20	Germany	Outpatients	Chronic DSM-IV	HRSD	Individual	M/Mo/T
	SP	111			20						
Schramm (2008)	IPT/medication	24	58.3	40.0 (10.77)	11	Germany	Inpatient	CHR or MDD+DYS	HRSD	Some group	M/Mo/T
	Medication/CM	21	76.2	45.9 (9.38)				DSM-IV			
Schramm (2011)	CBASP	13	57.1	40.2 (11.5)	22	Germany	Outpatient	Chronic DSM-IV	HRSD	Individual	M/Mo/T
	IPT	13	53.3		22						

Author Year	Intervention	N	Sex (% female)	Age (Years)	Planned (sessions)	Country	Recruited	Type of Depression	Depression Measure	Group or Individual	Treatment quality
Strauss (2012)	PBCT/TAU	14	71.4	43 (10.6)	12	UK	Outpatient	Chronic DSM-IV	BDI-II	Group	Mo/T
	TAU	14									
Wiersma (2014)	CBASP	53	68.7	41.1 (10.8)	24	Netherlands	Outpatient	Chronic DSM-IV	IDS	Individual	M/Mo/T
	CAU	57	51.4	43.0 (10.1)	22						

Key:

M = Manualised treatment, Mo = Monitored treatment, T = Trained therapists, CBT = Cognitive behavioural therapy, IPT = Interpersonal therapy, NR = Not reported, HRSD = Hamilton rating scale for depression, MADRS = Montgomery Ashberg Depression Rating Scale, DYS = Dysthymia, CHR = chronic, W/L = Wait List, TAU = Treatment as usual, MDD = Major depressive disorder, CT = cognitive therapy with out behavioural part, BDI-II = Beck Depression , SIPT = Spiritual Integrated Psychotherapy, HAM-D = Hamilton rating scale for depression, LTPP = Long term psychoanalytic psychotherapy, BSP = Brief supportive therapy, SP = Non-specific supportive psychotherapy, CHR = chronic depression, CM = Clinical management, Chronic DSM-IV = fits criteria of …., PBCT = Person based Cognitive Therapy, CAU = Care as usual, IDS = Inventory of depressive symptomology

1.4.1.1 Sex

All but one study reported sex data (Agosti et al., 1997) and percentage of female ranged from 31% to 80% with a mean (SD) of 59.42% (11.14).

1.4.1.2 Age

Age data was reported in all studies except de Mello et al., (2001) and Ravindran et al., (2000), while standard deviations were not reported in Dunner et al., (1996), Harpin et al., (1982), Markovitz et al., (2008). The average mean (SD) age of participants of studies that provided sufficient age data was 43.13 (11.71).

1.4.2 Group versus Individual therapies

There were 4 studies in which the psychological treatment was delivered in a group format with two other studies utilising a mixed format of both individual and group elements (de Jong et al., 1986 & Schramm et al., 2008). These studies were included in the group analysis since it was assumed that any benefit from the group format would be included in these. A moderator analysis of type of delivery of therapy (group or individual) (Table 2. & Figure 6.) gave a small mean effect size for individual therapy (14 studies with 31 different arms) d= 0.27 (95% CI: -0.42, -0.11), Z=3.34, (p<0.001), and heterogeneity was I^2=77% (p<0.001) compared with a moderate mean effect size for group delivery (6 studies with 13 different arms) d=-0.53 (95% CI: -0.80, -0.26) Z= 3.83 (p<0.001) and heterogeneity of I^2=60% (p<0.01). Testing for subgroup differences highlighted there was a significant difference between individual and group therapy using the p-value of 0.10 to assess for heterogeneity (I^2 = 63.3%, p=0.10) (Higgins et al., 2003; Deeks et al., 2021). (see Appendix B. for Forest plots).

A sensitivity analysis was performed by removing the studies which had group *and* individual treatment (de Jong et al., 1986 & Schramm et al., 2008). This did not have any significant impact on the result but increased the heterogeneity from I^2 = 60% to I^2 = 69% and a change in ES from *d* = 0.53 to *d* = 0.51. Using one ES per data set (highest and lowest) did not change the overall result with an advantage for group over individual therapy, but there were still high rates of heterogeneity and non-significant differences between the subgroups of group and individual treatment. A sensitivity analysis examining outliers was performed. In the individual analysis outliers were identified (Ebrahimi et al., (2013) CBTvW/L and SIPT v WL, Browne et al. (2002) (IPT), and Markovitz et al. (2005) IPT v MED. In the group treatment subgroup outliers were removed (Strauss et al., (2012), Ravindran et al. (2000) CBT v MED. The effect of removing the outliers reduced the heterogeneity from high to moderate in individual treatment and from high to zero heterogeneity in the group treatment subgroup. It did not have a significant effect on the mean effect size for each but did give a significant effect of difference between the two subgroups in the test for subgroup differences (I^2=87.1%, *p*=0.005).

1.4.2.1 Dysthymia or chronic depression subgroup analysis

1.4.2.1.1 Dysthymia

A subgroup analysis was performed to look at the moderating effect of type of depression (dysthymia or chronic depression). In the dysthymia subgroup of group treatment there was only one study with 5 arms (Ravindran et al., 2000) and the overall result was non-significant (*d*=-0.29, (95% CI: -0.80, 0.23), *Z*=1.10^{ns}, I^2=75%). While for individual treatment there was a moderate effect size (*d*=-0.42 (-0.79, -0.06), *Z*=2.26 (*p*<0.05), I^2=86% (*p*<0.001). A subtest analysis revealed there was no difference between the individual and group treatment for dysthymia (I^2=0%, *p*=0.67).

1.4.2.1.2 Chronic depression

In the chronic depression subgroup of group treatment there were 5 studies with 8 arms of comparisons showing mean effect size *d*=-0.67 (95 CI: -0.95, -0.39), *Z*=4.64, (*p*<0.001). Heterogeneity was lower than all group studies at I^2=35%^{ns}. A sensitivity analysis was performed taking out each study to observe any differences and taking Strauss et al. (2012) out brought heterogeneity to 0% and reducing the mean effect size from *d*=0.67 to *d*=0.55.

In chronic depression individual treatment subgroup (10 studies with 17 arms) there was a smaller but significant effect of *d*=-0.24 (95% CI: -0.37, -0.12) with moderate heterogeneity than for all individual studies (I^2=48%). Completing a sensitivity analysis in this subgroup by removing Keller et al. (2000) CBASP arm reduced heterogeneity to I^2=20% and mean effect size from *d* =0.24 (95% CI: -0.37, -0.12) to *d*=-0.30 (95% CI: -0.41, -0.20).

1.4.2.2 Active versus inactive controls

Analysis was performed by separating active controls (other therapy, medication) and inactive controls (waiting list (W/L), TAU, CAU, placebo).

1.4.2.2.1 Active control

Active controls in individual treatment subgroup (11 studies with 24 arms) and group treatment subgroup (3 studies with 5 arms) gave a small mean effect size (individual *d*=-0.18 (95% CI: -0.33, -0.04), group *d*=-0.21 (95% CI: -0.63, 0.22) but this was non-significant in the group treatment subgroup. There were no differences between the individual and group treatment groups (I^2=0%, *p*=0.92). A sensitivity analysis delivered no meaningful difference in the outcome except with group treatment when Ravindran et al. (2000) CBTvMED was removed which changed the mean effect size to a significant one and heterogeneity to 0% (*d*=-0.39 (95% CI: -0.67, -0.12), I^2=0%^{ns}), while this did increase heterogeneity between the subgroups this change was not significant (I^2=44.4%, *p*=0.18). With active controls in all comparisons there was no difference between individual and group. Only one outlier was found

(Markovitz et al., (2005) IPTvMED and this decreased heterogeneity by 2% to 65%.

1.4.2.2.2 Inactive controls

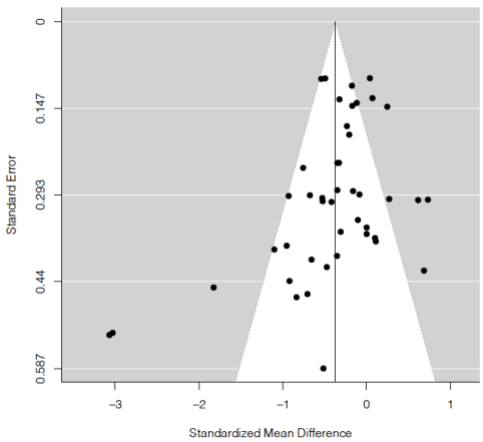
Comparing group (5 studies and 8 arms) and individual treatment (5 studies and 7 arms) inactive controls delivered large mean effect sizes compared with active controls ((individual *d*=-0.88 (95% CI: -1.59, -0.17), group *d*=-0.74 (95% CI: -1.03, -0.46). Like the active controls, there was no difference between the subgroups (I^2=0%, *p*=0.60).

An exploratory analysis of removing the dysthymia studies (Ebrahimi et al., (2013) individual, Ravindran et al., (2000) group) was performed and reduced the mean effect size and heterogeneity of the individual treatment subgroup to *d*=-0.18 (95% CI: -0.40, 0.04), I^2=0%, *p*=0.86, and made the result non-significant. The removal of Ravindran et al., (2000) increased the mean effect size of the group treatment subgroup (*d*=-0.81 (95% CI: -1.18, -0.43) and this delivered a significant difference between the subgroups of inactive/chronic depression in favour of group treatment (I^2=87.4%, *p*=0.005). A sensitivity analysis showed no meaningful differences of any other study arms being removed.

1.4.3 Publication bias

Publication bias was not found to be prevalent despite using different analysis techniques (see Appendix A. for Funnel plots). A trim and fill analysis using L0 and Q0 variable suggested there were no missing studies (Figure 3 & 4.), however, using R0 there were two studies highlighted as “missing” but this did not significantly change the result. Funnel plot asymmetry was assessed using a weighted regression test with multiplicative dispersion using standard error as a predictor yielded a non-significant result (test for funnel plot asymmetry: *t*

*(*42)=-1.8308, *p*=0.0742). A file drawer analysis using the Rosenthal (1995) approach (Fail safe N: 1268) also indicated that a large number of non-significant studies would not affect the overall meta-analysis result (Oswald & Plonsky, 2010). Furthermore, using a weight function model for publication bias gave an insignificant likelihood ratio test (X^2(d.f. = 1) = 0.3085674, *p*=0.57856 not indicating publication bias (Vevea & Hedges, 1995).



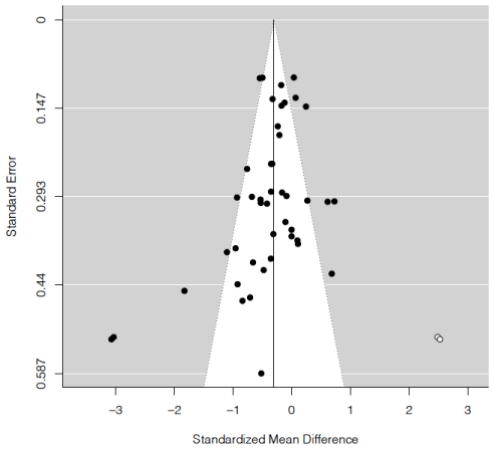


Figure 3. Trim and fill analysis (L0) ***Figure 4. Trim and fill analysis (R0)***

1.4.4 Quality of included studies

A sample of studies were co-rated for risk of bias by the second author. Inter-rater reliability was 80% for scoring risk of bias. The agreement was moderate Kappa=0.412, and greater than expected by chance (z=2.38, *p*=0.0174) (Landis & Koch, 1977). Risk of bias was assessed using RoB2 software (Sterne et al., 2019) (Figure 5.) One study was “low” risk, nine studies had “some concerns” and 10 with “high risk” of bias. “Measurement of the outcome” category showed least risk of bias with only one study with high risk and four with some concerns. “Deviations from the intended interventions” was next least problematic with four studies high risk and one some concerns. “Missing outcome data” with 7 high risk and one some concerns. “Randomization process” had eight studies at a low risk of bias (4 high risk and 8 some concerns) and “Selection of the reported result” had the least amount of low risk studies 4, 2 high risk and 14 some concerns).

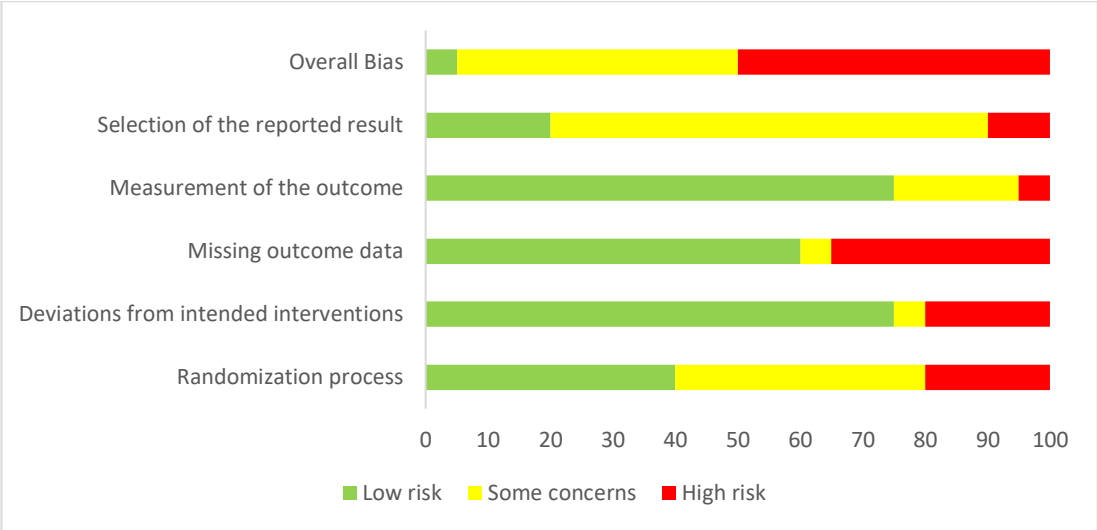


Figure 5. Risk of bias summary

Table 2. Meta-analysis results for individual versus group therapy

Comparison	No. of studies (arms)	Cohen's *d*	95% CI	Z score	I^2	*p* (between subgroups)	I^2 (between subgroups)
Individual versus group treatment							
Individual treatment	14 (31)	-0.27	-0.42, -0.11	3.34***	77%***	0.10	63.3%
Individual treatment outliers removed	14 (27)	-0.23	-0.35, -0.11	3.85***	52%***	0.005	87.1%
One ES per data set - highest	14 (17)	-0.32	-0.51, -0.12	3.16**	68%***	0.09	65.4%
One ES per data set - lowest	14 (17)	-0.22	-0.45, 0.00	1.96^{o}	74%***	0.18	44.9%
Group treatment	6 (13)	-0.53	-0.80, -0.26	3.83***	60%**	0.10	63.3%
Group treatment outliers removed	6 (11)	-0.53	-0.71, -0.35	5.88***	0%	0.005	87.1%
One ES per data set - highest	6 (7)	-0.67	-1.03, -0.31	3.68***	51%^{o}	0.09	65.4%
One ES per data set - lowest	6 (7)	-0.61	-1.13, -0.09	2.32**	76%***	0.18	44.9%
Subgroup Dysthymia							
Individual treatment	4 (14)	-0.42	-0.79, -0.06	2.26*	86%***	0.67	0%
One ES per data set - highest	4 (6)	-0.49	-1.18, 0.19	1.42^{ns}	87%***	0.50	0%
One ES per data set - lowest	4 (6)	-0.40	-1.19, 0.39	1.00^{ns}	90%***	0.78	0%
Group treatment	1 (5)	-0.29	-0.80, 0.23	1.10^{ns}	75%**	0.67	0%
One ES per data set - highest	1 (2)	-0.22	-0.62, 0.18	1.08^{ns}	0%^{ns}	0.50	0%
One ES per data set - lowest	1 (2)	-0.16	-1.67, 1.35	0.21^{ns}	92%***	0.78	0%

Comparison	No. of studies (arms)	Cohen's *d*	95% CI	Z score	I^2	*p* (between subgroups)	I^2 (between subgroups)
Subgroup chronic depression							
Individual treatment	10 (17)	-0.24	-0.37, -0.12	3.78***	48%*	0.007	86.2%
One ES per data set - highest	10 (11)	-0.33	-0.44, -0.22	6.01***	2%^{ns}	0.006	86.5%
One ES per data set - lowest	10 (11)	-0.14	-0.25, -0.03	2.50*	0%^{ns}	0.010	85.1%
Group treatment	5 (8)	-0.67	-0.95, -0.39	4.64***	35%^{ns}	0.007	86.2%
One ES per data set - highest	5 (5)	-0.89	-1.27, -0.50	4.52***	31%^{ns}	0.006	86.5%
One ES per data set - lowest	5 (5)	-0.78	-1.25, -0.31	3.24**	54%^{o}	0.010	85.1%
Subgroup Active control							
Individual treatment	11 (24)	-0.18	-0.33, -0.04	2.48*	69%***	0.92	0%
One ES per data set - highest	11 (12)	-0.27	-0.45, -0.09	2.94**	52%*	0.25	25.5%
One ES per data set - lowest	11 (12)	-0.06	-0.26, 0.14	0.59^{ns}	58%**	0.94	0%
Group treatment	3 (5)	-0.21	-0.63, 0.22	0.95^{ns}	65%*	0.92	0%
One ES per data set - highest	3 (3)	-0.48	-0.79, -0.17	3.05**	0%^{ns}	0.25	25.5%
One ES per data set - lowest	3 (3)	-0.09	-0.74, 0.56	0.27^{ns}	76%*	0.94	0%
Subgroup Inactive control							
Individual treatment	5 (7)	-0.88	-1.59, -0.17	2.43*	88%***	0.73	0%
One ES per data set - highest	5 (5)	-0.67	-1.36, 0.01	1.92^{o}	85%***	0.66	0%
One ES per data set - lowest	5 (5)	-0.65	-1.34, 0.04	1.84^{o}	85%***	0.60	0%

Comparison	No. of studies (arms)	Cohen's *d*	95% CI	Z score	I^2	*p* (between subgroups)	I^2 (between subgroups)
Group treatment	5 (8)	-0.74	-1.03, -0.46	5.07***	34%^{ns}	0.73	0%
One ES per data set - highest	5 (5)	-0.85	-1.29, -0.42	3.84***	47%^{ns}	0.66	0%
One ES per data set - lowest	5 (5)	-0.87	-1.35, -0.40	3.65***	54%^{o}	0.60	0%
Subgroup Risk of bias high risk							
Individual treatment	8 (21)	-0.35	-0.62, -0.08	2.58*	76%***	0.88	0%
One ES per data set - highest	8 (11)	-0.36	-0.75, 0.03	1.80^{o}	75%***	0.88	0%
One ES per data set - lowest	8 (11)	-0.35	-0.78, 0.09	1.55^{ns}	79%***	0.87	0%
Group treatment	2 (7)	-0.39	-0.81, 0.03	1.83^{o}	66%**	0.88	0%
One ES per data set - highest	2 (3)	-0.32	-0.69, 0.05	1.70^{o}	0%^{ns}	0.88	0%
One ES per data set - lowest	2 (3)	-0.30	-0.67, 0.07	1.60^{ns}	0%^{ns}	0.87	0%
Subgroup Risk of bias some/low risk							
Individual treatment	6 (10)	-0.20	-0.39, -0.02	2.15*	79%***	0.02	81.4%
One ES per data set - highest	6 (6)	-0.34	-0.49, -0.20	4.57***	29%^{ns}	0.02	80.3%
One ES per data set - lowest	6 (6)	-0.12	-0.33, 0.09	1.08^{ns}	62%*	0.03	79.2%
Group treatment	4 (6)	-0.67	-1.02, -0.32	3.78***	52%^{o}	0.02	81.4%
One ES per data set - highest	4 (4)	-0.92	-1.39, -0.44	3.78***	48%^{ns}	0.02	80.3%
One ES per data set - lowest	4 (4)	-0.81	-1.39, -0.23	2.72**	66%*	0.03	79.2%

Key:

o: p<0.10; *: p<0.05; **: p<0.01; ***: p<0.001. ^{ns}= non-significant.

N=number of studies, arms = number of comparisons

ES = effect size

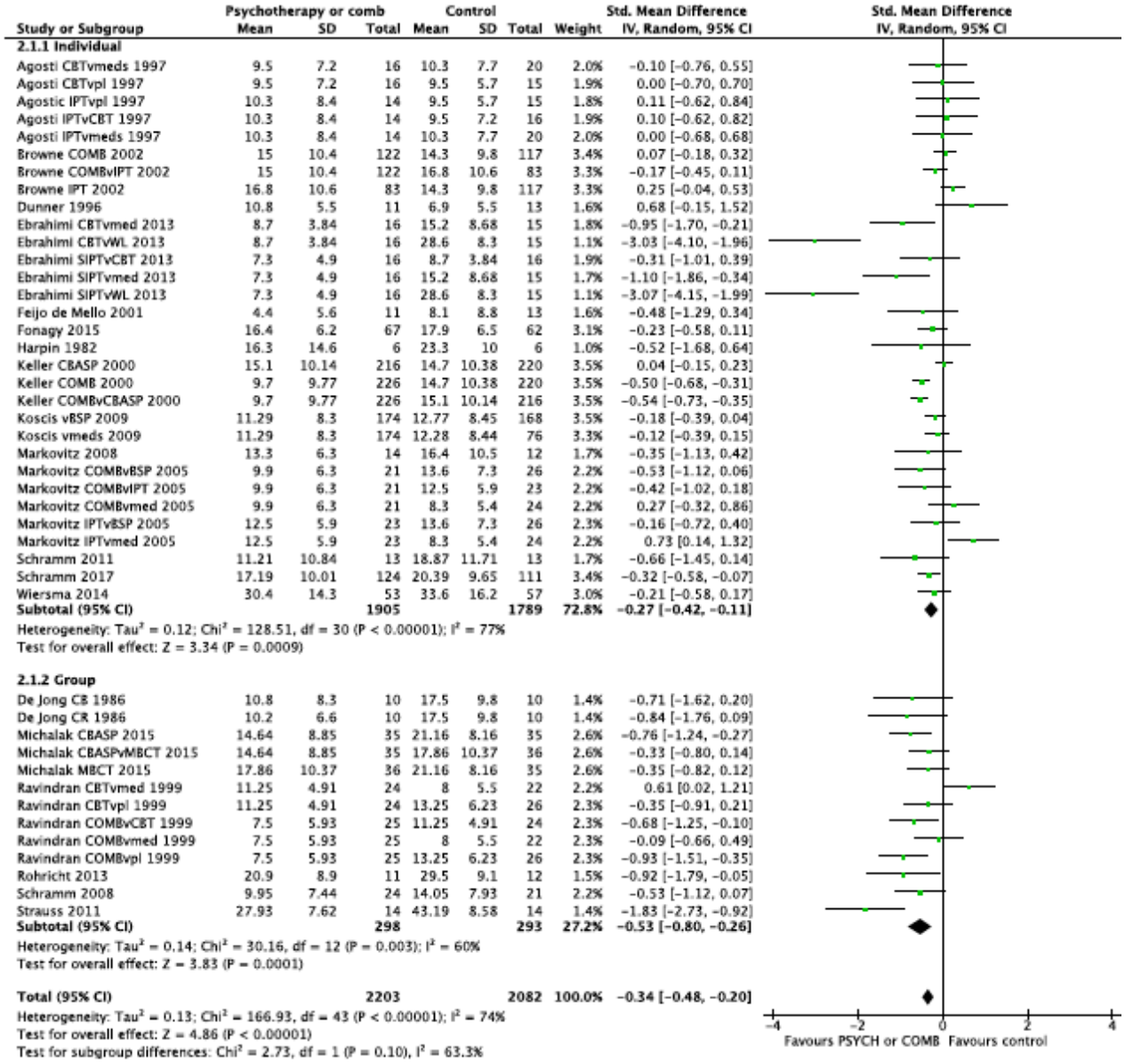


Figure 6. Forest plot of group versus individual therapy.

1.4.4.1.1 Active and inactive controls

Active and inactive controls were analysed for the whole data set. A moderator analysis of control type displayed a larger effect for inactive controls (*d*=-0.80 (-1.16, -0.44), *Z*=4.36 (*p*<0.001), I^2=79% (*p*<0.001) compared to active controls (*d* =-0.19 (-0.32, -0.05), *Z*=2.72 (*p*<0.01), I^2 = 67% (*p*<0.001) and confirmed the groups were statistically different. Comparing best case and worst-case scenario using one data set found a non-significant result for lowest data sets for active control, the difference between the subgroups held for all comparisons. Removing the inactive outliers (Ebrahimi et al., (2013) W/L arms) reduced the effect size from high to moderate (*d*=-0.50 from *d*=-0.88) and was still significant, with a significant difference between groups. Removing the active outliers (Ravindran et al., (2000) CBTvMED, Markovitz et al., (2005) IPTvMED, Browne et al., (2002) IPT, Keller et al., (2000) COMBvCBASP, Ebrahimi et al, (2013) SIPTvMED) maintained a significant effect and significant difference between the subgroups. Heterogeneity dropped from high to moderate by taking outliers out for both active and inactive subgroups. This held true with largest and smallest ES from study, though at worst case the ES is non-significant for active control.

1.4.4.1.2 Chronic or dysthymia

Analysis of type of depression was performed for the whole dataset. A moderator analysis for type of depression (chronic or dysthymia) produced similar effect size *d*=-0.38 (-0.68, -0.08) *Z*=2.49 (p<0.05), I^2 = 84% (p<0.001) dysthymia and chronic depression *d*=-0.33 (-0.46, -0.21), *Z*=5.16 (*p*<0.001), I^2=53% (*p*<0.01). There was less heterogeneity among the chronic depression studies (moderate compared to high) than the dysthymia studies. Testing for one ES per data set did not change the result significantly but the *Z* scores for dysthymia were non-significant. There was no heterogeneity between the depression groups indicating they were not significantly different. When comparing all the studies by type of diagnosis there was a small to medium

effect size which was significant but no difference between the subgroups. Removing the outliers (dysthymia – Ebrahimi et al., (2013) x W/L, Ravindran et al., (2000) CBTvMED, Markovitz et al., (2005) IPTvMED, Browne et al., (2002) IPT and chronic depression – Strauss et al., (2012), Keller et al., (2000) CBASP) made no significant difference to ES but lowered the heterogeneity and maintained there was no significant difference between the subgroups.

1.5 Discussion

1.5.1 Main findings

This meta-analysis was designed to investigate if there is any advantage to psychotherapy in a group format, for people with PDD, compared with individual therapy. The main results support there is a difference between the group and individual therapies for PDD but there are many factors to consider. These are summarised below with the implications for theory, strengths and limitations and finally directions for future research are explored.

1.5.1.1 Group versus individual treatment

This analysis found a significant difference in the efficacy of group treatment for PDD compared to the individual treatments, with group treatment giving a moderate effect size and individual a small effect size. The difference between the groups was substantial and significant, but the heterogeneity within the group and individual treatments was significant. Removing the outliers reduced the heterogeneity for group treatment suggesting those results are consistent with each other. The majority of outliers were treatment for dysthymia and this could support that dysthymia should be considered separately from other types of PDD (Rhebergen & Graham, 2014).

1.5.1.1.1 Chronic depression and dysthymia subgroups

The chronic depression subgroup maintained the significant finding and increased the effect size of group treatment to moderate to large. Using the highest ES maintained this result increasing effect size and lowest ES increased the group effect size to large and made individual treatment non-significant. The dysthymia subgroup was non-significant with no discernible difference between them, but with only one study in group treatment this comparison should be disregarded due to lack of power.

1.5.1.1.2 Inactive and active controls

The inactive controls gave a significant large effect for both group and individual therapy with no difference between the groups, however, there was significantly less heterogeneity in the group treatment suggesting the group study effects are more similar than the individual ones. Removing the outlier (Ebrahimi et al., 2013) made the individual treatment subgroup effect non-significant and made the difference between the individual and group treatment significant. Exploratory analysis revealed that inactive controls in treatment for chronic depression maintained a significant difference between group and individual treatment, with the individual effect non-significant. For active controls group treatment had a non-significant effect with no significant difference between the groups. Using highest ES made the results significant for both with a small effect for individual treatment and a moderate effect for group, but no difference between subgroups. There were 5 dysthymia studies in this analysis and a significant outlier (Ravindran et al., 2000). However, there were only 3 studies in the group treatment subgroup meaning the results should be considered with caution.

1.5.1.1.3 Risk of bias

The studies with a high risk of bias were homogenous and delivered a small to moderate effect size for both individual and group treatment but this was

not significant for group treatment. Studies with a lower risk of bias showed a significant difference between the group and individual treatment with a small effect for individual and moderate to large effect for group.

1.5.2 Theoretical implications

There was an overall small to moderate effect size for psychotherapy for PDD in all 20 studies and this compares with previous research (Cuijpers et al., 2010; Furukawa et al., 2018). This meta-analysis found a difference in favour of group treatment between overall group and individual treatment effects for PDD. Importantly, the lower risk of bias studies maintained the significant advantage of group over individual psychological therapy indicating that high quality studies were more likely to reveal group benefits. This is different to Cuijpers et al. (2019) finding that for CBT for MDD group treatment is equitable with individual treatment and could suggest that there is an advantage in offering group treatment to those with PDD but the result is to be taken with caution. The impact of outliers, poor quality and high-risk studies, dysthymia as a concept and type of active or inactive control appears significant. Many of the subgroup analyses are on a low number of studies and cannot be extrapolated.

The reasons for the advantage of group therapy in this sample could be attributed to interpersonal benefits and positive peer impacts and further studies could be designed to test this out (Fellin, et al., 2019, Lewinsohn & Clarke; 1999, Morrison 2001, Yalom & Leszcz, 2005). This could challenge the dominance of individual treatment for PDD when group treatments are additionally acceptable and effective with added benefits of reduced cost and therapist time (Cuijpers et al., 2019; Morrison, 2001; Tucker & Oei, 2007). Concerns over negative interpersonal traits may contribute to many people not being considered for group treatment, as those assessing for treatment might

have concerns about group dynamics or a person being able to tolerate a group (Constantino et al., 2008; Constantino et al., 2012; Leader & Klein, 1996). Group treatment for PDD includes evidence from CBASP which is tailored to deal with these issues (Sayegh et al., 2012; Locke et al., 2016), so any potential resistance or interpersonal problems (e.g. hostility or submissiveness) can be successfully overcome in a group environment (Locke et al. 2016). CBASP theory suggests that interpersonal change follows skill acquisition of the key skills of interpersonal learning in CBASP and that this is what leads to decrease in depressive symptoms; it is possible this could be maximised by peer connections in a group environment (McCullough et al., 2020) and this also fits with the theory of Yalom & Leszcz (2005). Nonetheless, group interventions are not tailored to the individual, and group dynamic problems can indeed disrupt progress in therapy while some may have difficulties disclosing personal information in front of others (Morrison, 2001; Tucker, 2007).

There was mixed evidence for group and individual treatment compared with active treatments (other therapy and medication) for PDD, with a small non-significant effect in group. However, a large proportion of the studies in this subgroup were treatment for dysthymia and this fits with Cuijpers et al. (2010) findings that suggest dysthymia is less receptive to psychotherapy treatment and might benefit more from medication. Dysthymia studies appeared to have a different effect and it is possible that different mechanisms in the development of dysthymia at play link to neurotic or anxiety co-morbidity (Hidalgo et al., 2012; Klein et al., 2000; Rhebergen & Graham, 2013).

1.5.3 Strengths and Limitations

This study collates the current available evidence comparing group and individual treatment for PDD and gives tentative results that there could be an advantage for group psychotherapy for PDD over individual psychotherapy.

Yet, the preliminary findings should be considered with care as this study does have several limitations. The conceptualisation of chronic depression and dysthymia has been chosen with the specified criteria from DSM-5 but other studies may categorise it differently or include terms such as TRD. While the studies were checked that they met the criteria for PDD it was often not clear in the research papers and some studies may have been discarded unnecessarily. Two studies which were outliers used the self-report BDI-II instead of the therapist measured HRSD-17, and it is possible that bias could affect either measure and this should be controlled for.

This meta-analysis found a broad mixture of treatments for PDD. Unfortunately, there were too few samples to be able to compare types of treatment by group and individual therapy, and it would be useful to know which therapies used an interpersonal element as recommended (Jobst et al., 2015) as they may have an added an advantage. Interpersonal behaviours such as hostility and submissiveness are not addressed in some therapies for PDD like IPT while CBASP addresses them directly (Schramm et al., 2015) and assessing such moderators and mediators of change would be beneficial. Likewise, it was not possible to explore further moderators such as type of control condition. The dose of therapy is another important feature in the literature and with only a third of the 20 studies reaching the recommended 18 sessions; understanding the impact of number of sessions as a moderator was not addressed in this study (Cuijpers et al., 2010; Schramm et al., 2019).

Due to the lack of follow up information available it was not possible to look at long term effect or remissions rates by group or individual therapy. Indeed, dropout was not considered in this study. With rates of support for people with depression already low (Wang et al., 2007), combined with treatment resistance and higher dropout rates in PDD (DeCarlo et al., 2016; Keller et al., 2014) this is another limitation of this meta-analysis. Unfortunately, many of

the studies were of poor quality and half were at an overall high risk of bias. Studies had a lack of clarity in reporting protocols, the randomisation process, and with issues such as missing outcome data, and selective reporting. These areas must be addressed to ensure research findings are rigorous and robust with minimal bias. The studies are in the main from Europe and the US and therefore, may not be generalisable out-with this area. Conversely, the contextual differences of the studies are wide ranging from type of therapy, recruitment of participants (clinical, outpatient, inpatient), to number of sessions offered. This raises the question if these differences are so significant that the studies might not be meaningful compared. Additionally, it could be argued that in comparing treatments for PDD and separating by mode of delivery the high heterogeneity means the meta-analysis could be comparing two completely different things; however, the exploratory nature of this study is thought to be useful to survey the evidence and possibly highlight directions for further research in this field (Field, 2005). Although the analysis did not indicate publication bias there was not a rigorous screening of the grey literature and since 12 studies could not be used due to insufficient information there was a third of studies missing at least. Indeed, the issue of “file drawer” (Field, 2005) where studies do not get published unless they have a positive result may mean any evidence of effect should be taken with extreme caution.

1.5.4 Future research considerations

This meta-analysis demonstrated an advantage in favour of group psychological therapy over individual therapy for PDD. However, the review also highlights the limitations of the evidence base and the need for further high-quality research. This would allow comparisons of different types of group interventions and controls that were not possible here. Attention should be directed to exploring the differences in the response of dysthymia and understanding the patient group better. Additional focus on length of treatment and follow up is important to make sure any change in depression is maintained long term. The majority of studies in this meta-analysis used the

HDRS-17 or BDI-II depression measures and since rates of anti-depressant use is climbing with associated risks of side effects and withdrawal symptoms that are linked to these questionnaires, the impact of any effect of using these measures is not known but should be considered in future studies (Hieronymus et al., 2021; Kendrick et al., 2021; NHS Digital, 2019; Saha et al., 2021). Research is required to understand the mechanisms of treatment for PDD in a more comprehensive way. This should include the impact that interpersonal variables have, for instance, measuring the specific interpersonal process of change that may be facilitated by group interactions and environments. It is hoped this could help conceptualise the apparent differences in treatment efficacy for dysthymia and allow for fine tuning or personalised treatment for those with PDD by taking into account moderators (such as childhood maltreatment, early or late onset, interpersonal traits). Lastly, it is important that studies also examine the efficacy of the implementation of RCT's into clinical practice to improve the provision for those who have PDD and ensure they get the ongoing evidence-based support that is recommended (Arnow & Constantino, 2003; Riihimaki et al., 2017; Schindler et al., 2011).

1.6 References

Agosti, V. & Ocepek-Welikson, K. (1997). The efficacy of imipramine and psychotherapy in early-onset chronic depression: a reanalysis of the National Institute of Mental Health Treatment of Depression Collaborative Research Program. *Journal of affective disorders, 43*(3), 181-186. doi:10.1016/S0165-0327(97)01428-6

American Psychiatric Association (2013): Diagnostic and Statistical Manual of Mental Disorders: *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition. Arlington, VA: American Psychiatric Association.

Arnow, B. A. & Constantino, M. J. (2003). Effectiveness of psychotherapy and combination treatment for chronic depression. *Journal of clinical psychology, 59*(8), 893-905. doi:10.1002/jclp.10181

Bird, T., Tarsia, M. & Schwannauer, M. (2018). Interpersonal styles in major and chronic depression:A systematic review and meta-analysis. *Journal of Affective Disorders*. 239, p. 93-101.

Browne, G., Steiner, M., Roberts, J., Gafni, A., Byrne, C., Dunn, E., et al. (2002). Sertraline and/or interpersonal psychotherapy for patients with dysthymic disorder in primary care: 6-Month comparison with longitudinal 2-year follow-up of effectiveness and costs. *Journal of Affective Disorders, 68*(2-3), 317-330. doi:http://dx.doi.org/10.1016/S0165-0327%2801%2900343-3

Caspi, A., Houts, R. M., Ambler, A., Danese, A., Elliott, M. L., Hariri, A., et al. (2020). Longitudinal Assessment of Mental Health Disorders and Comorbidities Across 4 Decades Among Participants in the Dunedin Birth Cohort Study. *JAMA network open, 3*(4), e203221-e203221. doi:10.1001/jamanetworkopen.2020.3221

Cicchetti, D., & Barnett, D. (1991). Attachment organization in maltreated preschoolers. *Development and Psychopathology*, 3, 397–411.

Cohen, J. (1988). Statistical power analysis for the behavioral sciences, (2nd ed.). Hillsdale, NJ: Erlbaum.

Constantino, M., Marnell, M., Haile, A., Kanther-Sista, S., Wolman, K., Zappert, L., et al. (2008). INTEGRATIVE COGNITIVE THERAPY FOR DEPRESSION: A RANDOMIZED PILOT COMPARISON. *Psychotherapy, 45*(2), 122-134. doi:10.1037/0033-3204.45.2.122

Constantino, M. J., Laws, H. B., Arnow, B. A., Klein, D. N., Rothbaum, B. O. & Manber, R. (2012). The relation between changes in patients' interpersonal impact messages and outcome in treatment for chronic depression. *Journal of Consulting and Clinical Psychology, 80*(3), 354-364. doi:http://dx.doi.org/10.1037/a0028351

Cuijpers, P., Geraedts, M. A., van Oppen, P., Andersson, G., Markovitz, J. C., van Straten, A. (2011) Interpersonal Psychotherapy for Depression: A Meta-Analysis. *American Journal of Psychiatry.* 168, 581-591.

Cuijpers, P., Noma, H., Karyotaki, E., Cipriani, A. & Furukawa, T. A. (2019). Effectiveness and Acceptability of Cognitive Behavior Therapy Delivery Formats in Adults With Depression: A Network Meta-analysis. *JAMA psychiatry (Chicago, Ill.), 76*(7), 700-707. doi:10.1001/jamapsychiatry.2019.0268

Cuijpers, P., Noma, H., Karyotaki, E., Vinkers, C. H., Cipriani, A. & Furukawa, T. A. (2020). A network meta-analysis of the effects of psychotherapies, pharmacotherapies and their combination in the treatment of adult depression. *World Psychiatry, 19*(1), 92-107. doi:http://dx.doi.org/10.1002/wps.20701

Cuijpers, P., Sijbrandij, M., Koole, S. L., Andersson, G., Beekman, A. T. & Reynolds, I. C. F. (2013). The efficacy of psychotherapy and

pharmacotherapy in treating depressive and anxiety disorders: A meta-analysis of direct comparisons. *World Psychiatry, 12*(2), 137-148. doi:http://dx.doi.org/10.1002/wps.20038

Cuijpers, P., Sijbrandij, M., Koole, S. L., Andersson, G., Beekman, A. T. & Reynolds, I. C. F. (2014). Adding psychotherapy to antidepressant medication in depression and anxiety disorders: A meta-analysis. *World Psychiatry, 13*(1), 56-67. doi:http://dx.doi.org/10.1002/wps.20089

Cuijpers, P., van Straten, A., Schuurmans, J., van Oppen, P., Hollon, S. D. & Andersson, G. (2010). Psychotherapy for chronic major depression and dysthymia: A meta-analysis. *Clinical Psychology Review, 30*(1), 51-62. doi:http://dx.doi.org/10.1016/j.cpr.2009.09.003

Cuijpers et al., (2019) Open Science Framework (OSF) website. A meta-analytic database of randomised trials on psychotherapies for depression. Accessed: https://osf.io/825c6/

De Carlo, V., Calati, R. & Serretti, A. (2016). Socio-demographic and clinical predictors of non-response/non-remission in treatment resistant depressed patients: A systematic review. *Psychiatry Research, 240*, 421-430. doi:http://dx.doi.org/10.1016/j.psychres.2016.04.034

Deeks., J. J., Julian PT Higgins, Douglas G Altman; (2021) on behalf of the Cochrane Statistical Methods Group accessed: https://training.cochrane.org/handbook/current/chapter-10

de Mello, M. F., Myczcowisk, L. M. & Menezes, P. R. (2001). A randomized controlled trial comparing moclobemide and moclobemide plus interpersonal psychotherapy in the treatment of dysthymic disorder. *Journal of Psychotherapy Practice & Research 10(2):117-23, 2001 Spring, 10*(2), 117-123.

Dunner, D. L. (2001). Acute and maintenance treatment of chronic depression. *The journal of clinical psychiatry, 62*(6), 10-16.

Dunner D.L, Schmaling K.B, Hendrickson H, Becker J, Lehman A, Bea C. (1996). Cognitive therapy versus fluoxetine in the treatment of dysthymic disorder. Depression. 1996;4(1):34-41. doi: 10.1002/(SICI)1522-7162 4:1<34::AID-DEPR4>3.0.CO;2-F. PMID: 9160652.

Duval, S. & Tweedie, R. (2000). Trim and Fill: A Simple Funnel-Plot-Based Method of Testing and Adjusting for Publication Bias in Meta-Analysis. *Biometrics, 56*(2), 455-463. doi:10.1111/j.0006-341X.2000.00455.x

Ebrahimi, A., Neshatdoost, H. T., Mousavi, S. G., Asadollahi, G. A. & Nasiri, H. (2013). Controlled randomized clinical trial of spirituality integrated psychotherapy, cognitive-behavioral therapy and medication intervention on depressive symptoms and dysfunctional attitudes in patients with dysthymic disorder. *Advanced Biomedical Research 2:53, 2013, 2*, 53.

Egger, M., Smith, G. D., Schneider, M. & Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *BMJ, 315*(7109), 629-634. doi:10.1136/bmj.315.7109.629

Fava, M. (2003). Diagnosis and definition of treatment-resistant depression. *Biological psychiatry (1969), 53*(8), 649-659. doi:10.1016/S0006-3223(03)00231-2

Fellin, L.C., Callaghan, J.E., Alexander, J.H., Harrison-Breed, C., Mavrou, S., Papathanasiou, M., 2019. Empowering young people who experienced domestic violence and abuse: The development of a group therapy intervention. Clinical Child Psychology and Psychiatry 24, 170–189.. doi:10.1177/1359104518794783

Field, Andy. (2005) A Bluffer's Guide to Meta-Analysis. Accessed June 2021: http://www.discoveringstatistics.com/docs/meta.pdf

Fogarty, C., Hevey, D., Mccarthy, O., 2019. Effectiveness of cognitive behavioural group therapy for social anxiety disorder: long-term benefits and

aftercare. Behavioural and Cognitive Psychotherapy 47, 501–513.. doi:10.1017/s1352465819000079

Freedheim, D. K., Freudenberger, H. J., Kessler, J. W., Messer, S. B., Peterson, D. R., Strupp, H. H., & Wachtel, P. L. (Eds.). (1992). *History of psychotherapy: A century of change.* American Psychological Association. https://doi.org/10.1037/10110-000

Furukawa, T. A., Efthimiou, O., Weitz, E. S., Cipriani, A., Keller, M. B., Kocsis, J. H., et al. (2018). Cognitive-behavioral analysis system of psychotherapy, drug, or their combination for persistent depressive disorder: Personalizing the treatment choice using individual participant data network metaregression. *Psychotherapy and Psychosomatics, 87*(3), 140-153. doi:http://dx.doi.org/10.1159/000489227

Guidi, J. & Fava, G. A. (2020). Sequential Combination of Pharmacotherapy and Psychotherapy in Major Depressive Disorder: A Systematic Review and Meta-analysis. *JAMA psychiatry*. doi:http://dx.doi.org/10.1001/jamapsychiatry.2020.3650

Hamilton, W.K., & Mizumoto, A. (2017). MAVIS: Meta Analysis via Shiny. R package version 1.1.3.(accessed 2021 at: http://kylehamilton.net/shiny/MAVIS/).

Hamilton M. (1960). A rating scale for depression. *J Neurol Neurosurg* Psychiatry 1960.

Harpin, R. E., Liberman, R. P., Marks, I., Stern, R. & Bohannon, W. E. (1982). Cognitive-Behavior Therapy for Chronically Depressed Patients A Controlled Pilot Study. *The journal of nervous and mental disease, 170*(5), 295-301. doi:10.1097/00005053-198205000-00007

Hidalgo, R. B. & Sheehan, D. V. (2012). Generalized anxiety disorder. *Handbook of Clinical Neurology, 106*, 343-362. doi:10.1016/B978-0-444-52002-9.00019-X

Hieronymus, F., Lisinski, A., Eriksson, E. & Østergaard, S. D. (2021). Do side effects of antidepressants impact efficacy estimates based on the Hamilton Depression Rating Scale? A pooled patient-level analysis. *Translational psychiatry, 11*(1), 249-249. doi:10.1038/s41398-021-01364-0

Higgins, J. P., Thompson, S. G., & Deeks, J. J. (2003). Measuring inconsistency in metaanalyses. *British Medical Journal*, 327, 557–560.

Higgins JPT, Sterne JAC, Savović J, Page MJ, Hróbjartsson A, Boutron I, Reeves B, Eldridge S. A revised tool for assessing risk of bias in randomized trials In: Chandler J, McKenzie J, Boutron I, Welch V (editors). (2016) Cochrane Methods. *Cochrane Database of Systematic Reviews* 2016, Issue 10 (Suppl 1). dx.doi.org/10.1002/14651858.CD201601.

Higgins JPT, Li T, Deeks JJ (editors). Chapter 6: Choosing effect measures and computing estimates of effect. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). (2019) Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019). Cochrane, 2019. Available from https://training.cochrane.org/handbook/current/chapter-06#section-6-5-2 (table 6.5.2a)

Ijaz, S., Davies, P., Williams, C. J., Kessler, D., Lewis, G. & Wiles, N. (2018). Psychological therapies for treatment-resistant depression in adults. *Cochrane Database of Systematic Reviews, 2018*(5), CD010558. doi:http://dx.doi.org/10.1002/14651858.CD010558.pub2

Jobst, A., Brakemeier, E. L., Buchheim, A., Caspar, F., Cuijpers, P., Ebmeier, K. P., et al. (2015). European Psychiatric Association Guidance on psychotherapy in chronic depression across Europe. *European psychiatry, 33*(1), 18-36. doi:10.1016/j.eurpsy.2015.12.003

Keller, M. B., McCullough, J. P., Klein, D. N., Arnow, B., Dunner, D. L., Gelenberg, A. J., et al. (2000). A comparison of nefazodone, the cognitive behavioral-analysis system of psychotherapy, and their combination for the

treatment of chronic depression. *New England Journal of Medicine, 342*(20), 1462-1470. doi:http://dx.doi.org/10.1056/NEJM200005183422001

Keller, S. M., Feeny, N. C. & Zoellner, L. A. (2014). Depression Sudden Gains and Transient Depression Spikes During Treatment for PTSD. *Journal of consulting and clinical psychology, 82*(1), 102-111. doi:10.1037/a0035286

Kendrick, T. (2021). Strategies to reduce use of antidepressants. *British journal of clinical pharmacology, 87*(1), 23-33. doi:10.1111/bcp.14475

Klein, D. N., Schwartz, J. E., Rose, S. & Leader, J. B. (2000). Five-Year Course and Outcome of Dysthymic Disorder: A Prospective, Naturalistic Follow-Up Study. *The American journal of psychiatry, 157*(6), 931-939. doi:10.1176/appi.ajp.157.6.931

Kocsis, J. H., Gelenberg, A. J., Rothbaum, B., Klein, D. N., Trivedi, M. H., Manber, R., et al. (2008). Chronic forms of major depression are still undertreated in the 21st century: Systematic assessment of 801 patients presenting for treatment. *Journal of affective disorders, 110*(1), 55-61. doi:10.1016/j.jad.2008.01.002

Krystal, J. H., Rosenheck, R. A., Cramer, J. A., Vessicchio, J. C., Jones, K. M., Vertrees, J. E., et al. (2011). Adjunctive Risperidone Treatment for Antidepressant-Resistant Symptoms of Chronic Military Service–Related PTSD: A Randomized Trial. *JAMA : the journal of the American Medical Association, 306*(5), 493-502. doi:10.1001/jama.2011.1080

Köhler, S., Chrysanthou, S., Guhn, A. & Sterzer, P. (2019). Differences between chronic and nonchronic depression: Systematic review and implications for treatment. *Depression and anxiety, 36*(1), 18-30. doi:10.1002/da.22835

Landis, J. R. & Koch, G. G. (1977). The Measurement of Observer Agreement for Categorical Data. *Biometrics, 33*(1), 159-174. doi:10.2307/2529310

Leader, J. B. & Klein, D. N. (1996). Social adjustment in dysthymia, double depression and episodic major depression. *Journal of affective disorders, 37*(2), 91-101. doi:10.1016/0165-0327(95)00076-3

Lewinsohn, P. M. & Clarke, G. N. (1999). Psychosocial treatments for adolescent depression. *Clinical psychology review, 19*(3), 329-342. doi:10.1016/S0272-7358(98)00055-5

Lizardi, H., Klein, D. N., Ouimette, P. C., Riso, L. P., Anderson, R. L. & Donaldson, S. K. (1995). Reports of the Childhood Home Environment in Early-Onset Dysthymia and Episodic Major Depression. *Journal of abnormal psychology (1965), 104*(1), 132-139. doi:10.1037/0021-843X.104.1.132

Locke, K. D., Sayegh, L., Penberthy, J. K., Weber, C., Haentjens, K. & Turecki, G. (2017). Interpersonal Circumplex Profiles Of Persistent Depression: Goals, Self-Efficacy, Problems, And Effects Of Group Therapy. *Journal of clinical psychology, 73*(6), 595-611. doi:10.1002/jclp.22343

Markowitz, J. C., Kocsis, J. H., Bleiberg, K. L., Christos, P. J. & Sacks, M. (2005). A comparative trial of psychotherapy and pharmacotherapy for “pure” dysthymic patients. *Journal of affective disorders, 89*(1), 167-175. doi:10.1016/j.jad.2005.10.001

Markowitz, J. C., Kocsis, J. H., Christos, P., Bleiberg, K. & Carlin, A. (2008). Pilot Study of Interpersonal Psychotherapy Versus Supportive Psychotherapy for Dysthymic Patients With Secondary Alcohol Abuse or Dependence. *The journal of nervous and mental disease, 196*(6), 468-474. doi:10.1097/NMD.0b013e31817738f1

McCullough, J. J. P. (2020). Characteristics of the Optimal Cognitive Behavioral Analysis System of Psychotherapy (CBASP) Therapist Role. *Frontiers in psychiatry, 11*, 609954-609954. doi:10.3389/fpsyt.2020.609954

McHugh, R. K., Whitton, S. W., Peckham, A. D., Welge, J. A. & Otto, M. W. (2013). Patient preference for psychological vs pharmacologic treatment of

psychiatric disorders: A meta-analytic review. *The journal of clinical psychiatry, 74*(6), 595-602. doi:10.4088/JCP.12r07757

Moher, D., Liberati, A., Tetzlaff, J. & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ, 339*(7716), e78-336. doi:10.1136/bmj.b2535

Morrison, N. (2001). GROUP COGNITIVE THERAPY: TREATMENT OF CHOICE OR SUB-OPTIMAL OPTION? *Behavioural and cognitive psychotherapy, 29*(3), 311-332. doi:10.1017/S1352465801003058

Murphy, J. & Byrne, G. (2011). The failure to define: A systematic review of the conceptualisation of treatment resistant depression (TRD). *Australian and New Zealand Journal of Psychiatry, 45*(O1), A45.

Nanni, V., Uher, R. & Danese, A. (2012). Childhood Maltreatment Predicts Unfavorable Course of Illness and Treatment Outcome in Depression: A Meta-Analysis. *The American journal of psychiatry, 169*(2), 141-151. doi:10.1176/appi.ajp.2011.11020335

National Institute for Clinical Excellence, July 2017, draft for consultation. Depression in adults: treatment and management. Available at https://www.nice.org.uk/guidance/indevelopment/gid-cgwave0725 accessed May 2021.

NHS Digital. Prescription cost analysis data: NHS Digital; 2019.

https://digital.nhs.uk/data-and-information/publications/statistical/

prescription-cost-analysis/2018. Accessed May 29, 2020.

Office for National Statistics (ONS) (2021). Coronavirus and depression in adults, Great Britain: January to March 2021

Accessed May 2021:
https://www.ons.gov.uk/peoplepopulationandcommunity/wellbeing/articles/coronavirusanddepressioninadultsgreatbritain/januarytomarch2021

Oswald, F. L. & Plonsky, L. (2010). Meta-analysis in Second Language Research: Choices and Challenges. *Annual review of applied linguistics, 30*, 85-110. doi:10.1017/S0267190510000115

Pettit, J. W., Lewinsohn, P. M., Roberts, R. E., Seeley, J. R. & Monteith, L. (2008). The long-term course of depression: development of an empirical index and identification of early adult outcomes. *Psychological medicine, 39*(3), 403-412. doi:10.1017/S0033291708003851

Ravindran, A. V., Guelfi, J. D., Lane, R. M. & Cassano, G. B. (2000). Treatment of dysthymia with sertraline: A double-blind, placebo-controlled trial in dysthymic patients without major depression. *Journal of Clinical Psychiatry, 61*(11), 821-827. doi:http://dx.doi.org/10.4088/JCP.v61n1103

Review Manager (RevMan) [Computer program]. Version 5.4.1, The Cochrane Collaboration, 2020.

Rhebergen, D. & Graham, R. (2014). The re-labelling of dysthymic disorder to persistent depressive disorder in DSM-5: old wine in new bottles? *Current opinion in psychiatry, 27*(1), 27-31. doi:10.1097/YCO.0000000000000022

Riihimaki, K. (2017). Health-related quality of life of primary care patients with depressive disorders. *European psychiatry, 41*(S1), S540-S540. doi:10.1016/j.eurpsy.2017.01.747

Rosenthal, R. (1995). Writing Meta-analytic reviews. *Psychological Bulletin*, 118 (2), p. 183-192.doi 10.1037/0033-2909.118.2.183

Rubio, J. M., Markowitz, J. C., Alegría, A., Pérez-Fuentes, G., Liu, S. M., Lin, K. H., et al. (2011). Epidemiology of chronic and nonchronic major depressive disorder: results from the national epidemiologic survey on alcohol and related conditions. *Depression and anxiety, 28*(8), 622-631. doi:10.1002/da.20864

Saha, K., Torous, J., Kiciman, E. & De Choudhury, M. (2021). Understanding Side Effects of Antidepressants: Large-scale Longitudinal Study on Social Media Data. *JMIR mental health, 8*(3), e26589-e26589. doi:10.2196/26589

Sayegh, L., Locke, K. D., Pistilli, D., Penberthy, J. K., Chachamovich, E., McCullough, J. P., et al. (2012). Cognitive Behavioural Analysis System of Psychotherapy for Treatment-Resistant Depression: Adaptation to a Group Modality. *Behaviour change, 29*(2), 97-108. doi:10.1017/bec.2012.2

Schindler, A. C., Hiller, W. & Witthoft, M. (2011). Benchmarking of cognitive-behavioral therapy for depression in efficacy and effectiveness studies--how do exclusion criteria affect treatment outcome? *Psychotherapy research : journal of the Society for Psychotherapy Research, 21*(6), 644-657.

Schramm, E., Caspar, F. & Berger, M. (2006). A specific therapy for chronic depression. McCullough's Cognitive Behavioral Analysis System of Psychotherapy. *Nervenarzt, 77*(3), 355-370; quiz 371.

Schramm, E., Kriston, L., Elsaesser, M., Fangmeier, T., Meister, R., Bausch, P., et al. (2019). Two-year follow-up after treatment with the cognitive behavioral analysis system of psychotherapy versus supportive psychotherapy for early-onset chronic depression. *Psychotherapy and Psychosomatics, 88*(3), 154-164. doi:http://dx.doi.org/10.1159/000500189

Schramm, E., Schneider, D., Zobel, I., van Calker, D., Dykierek, P., Kech, S., et al. (2008). Efficacy of Interpersonal Psychotherapy plus pharmacotherapy in chronically depressed inpatients. *Journal of Affective Disorders, 109*(1-2), 65-73. doi:http://dx.doi.org/10.1016/j.jad.2007.10.013

Schramm, E., Zobel, I., Schoepf, D., Fangmeier, T., Schnell, K., Walter, H., et al. (2015). Cognitive behavioral analysis system of psychotherapy versus escitalopram in chronic major depression. *Psychotherapy and Psychosomatics, 84*(4), 227-240. doi:http://dx.doi.org/10.1159/000381957

Sheikh, A. (2018). Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017:a systematic analysis for the Global Burden of Disease Study 2017. *Sheikh , A 2018 , ' Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017 : a systematic analysis for the Global Burden of Disease Study 2017 ' , The Lancet , vol. 392 , no. 10159 , pp. 1789-1858 . https://doi.org/10.1016/S0140-6736(18)32279-7*. doi:https://doi.org/10.1016/S0140-6736(18)32279-7

Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng H-Y, Corbett MS, Eldridge SM, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT. (2019). RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*; **366**: l4898.

Strauss, C., Hayward, M. & Chadwick, P. (2012). Group person-based cognitive therapy for chronic depression: a pilot randomized controlled trial. *The British journal of clinical psychology / the British Psychological Society, 51*(3), 345-350.

The Matrix (2015). A Guide to Delivering Evidence-Based Psychological Therapies in Scotland. NHS Education Scotland (NES).

Torpey, D. C. & Klein, D. N. (2008). Chronic depression: Update on classification and treatment. *Current psychiatry reports, 10*(6), 458-464. doi:10.1007/s11920-008-0074-6

Trivedi, M. H., Rush, A. J., Wisniewski, S. R., Nierenberg, A. A., Warden, D., Ritz, L., et al. (2006). Evaluation of Outcomes With Citalopram for Depression Using Measurement-Based Care in STARD: Implications for Clinical Practice. *The American journal of psychiatry, 163*(1), 28-40. doi:10.1176/appi.ajp.163.1.28

Tucker, M. & Oei, T. P. S. (2007). Is Group More Cost Effective than Individual Cognitive Behaviour Therapy? The Evidence is not Solid Yet. *Behavioural and cognitive psychotherapy, 35*(1), 77-91. doi:10.1017/S1352465806003134

Vevea, J.L., Hedges, L.V. A general linear model for estimating effect size in the presence of publication bias. *Psychometrika* **60,** 419–435 (1995). https://doi.org/10.1007/BF02294384

Wang, P. S., Aguilar-Gaxiola, S., Alonso, J., Angermeyer, M. C., Borges, G., Bromet, E. J., et al. (2007). Worldwide Use of Mental Health Services for Anxiety, Mood, and Substance Disorders: Results from 17 Countries in the WHO World Mental Health (WMH) Surveys. *The Lancet (British edition), 370*(9590), 841-850. doi:10.1016/S0140-6736(07)61414-7

Wiersma, J. E., Hovens, J. G. F. M., van Oppen, P., Giltay, E. J., van Schaik, D. J. F., Beekman, A. T. F., et al. (2009). The Importance of Childhood Trauma and Childhood Life Events for Chronicity of Depression in Adults. *The journal of clinical psychiatry, 70*(7), 983-989. doi:10.4088/JCP.08m04521

Wiersma, J. E., Van Schaik, D. J. F., Hoogendorn, A. W., Dekker, J. J., Van, H. L., Schoevers, R. A., et al. (2014). The Effectiveness of the Cognitive Behavioral Analysis System of Psychotherapy for Chronic Depression: A Randomized Controlled Trial. *Psychotherapy and psychosomatics, 83*(5), 263-269. doi:10.1159/000360795

Wittchen, H. U., Jacobi, F., Rehm, J., Gustavsson, A., Svensson, M., Jönsson, B., et al. (2011). The size and burden of mental disorders and other disorders of the brain in Europe 2010. *European neuropsychopharmacology, 21*(9), 655-679. doi:10.1016/j.euroneuro.2011.07.018

World Health Organization. (2018). *International classification of diseases for mortality and morbidity statistics* (11th Revision). Retrieved from https://icd.who.int/browse11/l-m/en

World Health Organisation (WHO) (2020). Depression fact sheet. Accessed: https://www.who.int/news-room/fact-sheets/detail/depression

Yalom, I. D., & Leszcz, M. (2005). *The theory and practice of group psychotherapy*. New York: Basic Books.

Journal Article 2: Original research[1]

Evaluating the effectiveness and change processes of group Cognitive Behavioural Analysis System of Psychotherapy for persistent depression in an outpatient setting.

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[1] Written in accordance with guidelines for Journal of Affective Disorders

Chapter 2 Original research

2.1 Abstract

2.1.1 Introduction

Chronic/persistent depression is a debilitating condition which can be difficult to treat. Cognitive Behavioural Analysis System of Psychotherapy (CBASP) is a psychological treatment for persistent depression which has a solid evidence base. Little is known about the mechanism of change during CBASP. It is hypothesised that as learning acquisition increases in CBASP participants symptoms will improve.

2.1.2 Methods

To test out this hypothesis clinical outcome data from 13 groups of CBASP (CBASP-G) were analysed using multi-level modelling statistical methods and paired t-tests. Outcome data from 80 participants who attended CBASP-G for persistent depression between 2011 and 2021 in an outpatient primary care setting were entered into SPSS. Multi-level models were built to look for any pattern between skill acquisition in CBASP-G and weekly change in reported Mood and CORE-10 score. Paired t-tests were run to look at overall change in outcome data for BDI-II, CORE-10, Mood, IIP-32, PGI, CGI-I and CGI-S. Multiple imputation was used to deal with missing data for the t-tests.

2.1.3 Results

Paired t-tests and exact sign tests demonstrated that CBASP-G significantly improved depression (BDI-II $t(25)=4.181$, $p<0.001$, $d=0.820$), distress (CORE—10 $t(29)=3.034$, $p=0.005$, $d=0.554$), mood (t (35)=-3.768, $p=0.001$, $d=-0.628$, and global indicators of improvement scores. Changes in total IIP-32 were not significant but there was significant change in the hostile-

submissive domain (t(25)=3.433, *p*=0.002, *d*=0.673). Multiple imputation upheld the core findings of the t-tests. Multilevel models suggested that the change in distress and mood scores were linear during CBASP-G, that there was no regression to the mean over time pointing to an effect of therapy. Measures of skill acquisition (PQ-SA, PQ-IDE, PPRF) all improved the model fit significantly indicating they are important to an improvement in symptoms. However, only the fixed effect of PQ-SA for the CORE-10 model was significant and the PQ-SA*Time for the Mood model. Skill acquisition was quadratic in nature, with competency increasing at the start of therapy and then levelling off. The group attended may have had a small effect on the outcome for the CORE-10, however, there was not enough data to model the effect of the group for the mood scores.

2.1.4 Conclusions

CBASP-G in an outpatient setting had an effect in reducing depression and overall distress and increasing mood over the 20-week sessions; this is in line with previous research. Skill acquisition in CBASP-G is important to explaining the variance in symptoms, however, perhaps due to the small sample only PQ-SA was significant. Interpersonal change was present for hostile-submissive traits. There was a substantial amount of outcome data missing from this sample and there may be a lack of power to find proposed effects in IIP change and a link between skill acquisition over time. This study highlights that CBASP-G in practice in outpatient setting is effective and supports that the key learning acquisition of the situational analysis in CBASP is an important part of improving symptoms and interpersonal style.

Keywords: Chronic depression, Persistent Depressive Disorder, Multilevel Modelling, CBASP, skill acquisition.

2.2 Original research

2.2.1 Introduction

Most people will experience a mental health condition across their lifespan and the two most common are anxiety and depressive disorders (Caspi & Moffitt, 2020; World Health Organisation (WHO), 2020). Depression is the biggest reason for disability worldwide, can lead to suicide and its economic and social burden has made it a global health challenge (Hewlett et al., 2014; Wittchen et al., 2011; WHO, 2020). The Scottish Health Survey (2019) estimates that around 12% of people in Scotland report at least two symptoms of depression. More recently, in the first months of 2021 it is estimated that around 21% of adults across the UK report symptoms of depression (moderate to severe assessed by PHQ-8), almost twice the pre-COVID-19 pandemic level of 10% (ONS, 2021). Additionally, people with depression use 1.5 to 2 times health service resource than those without (Arnow & Constantino, 2003).

Chronic or persistent depression is classified as having depressive symptoms present for at least 2 years; the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) reclassified the four subtypes of chronic depression (chronic depression, dysthymia, double depression, recurrent depression without full remission) to an overarching persistent depressive disorder (PDD) which can be early or late onset (before or after age 21) (American Psychiatric Association, 2013). Around 30% of those with depression are thought to have PDD (Murphy & Byrne, 2012; Rubio et al., 2011). The International Classification of Diseases 11th revision (ICD-11) use a coding system to define the persistent element of MDD and use similar definitions of 2 years without remission (World Health Organization, 2018).

Persistent depression places a huge burden on strained health services, using a disproportionate amount of mental health services (Torpey & Klein, 2008). Indeed, the effect on the individual and those around them can be substantial with those with PDD having higher co-morbidity for mental health and medical problems and lower quality of life than those with episodic depression (Angst et al., 2008; Gilmer et al., 2005; Murphy & Byrne, 2012; Pettit et al., 2008). Additionally, there are delays and variability in people getting sufficient treatment for PDD and poorer outcomes from treatment than non-chronic depression (Jobst et al., 2015; Pettit et al., 2008; Rubio et al., 2011).

Cognitive Behavioural Analysis System of Psychotherapy (CBASP) is the only type of therapy that has been specifically designed to treat PDD through facilitating interpersonal change (McCullough, 2020). This paper will use data from participants with PDD who attended a group version of CBASP (CBASP-G) to examine the change processes and effectiveness of this group intervention. Moderating factors, limitations and directions for future research will be discussed.

2.2.2 Mechanisms in PDD

Research has attempted to explain likely contributors and mechanisms involved in the development and maintenance of chronic forms of depression but issues such as the classification of PDD and a lack of understanding of the course of depression across the lifespan have complicated the matter. (Neubel et al., 2020; Rhebergen & Graham, 2014).

2.2.2.1 Childhood maltreatment

There is evidence that childhood maltreatment (CM) (emotional/physical/sexual abuse, neglect) is a feature in the development of PDD (Cicchetti & Barnett, 1991; Klein et al., 2015; Nelson et al., 2017), with

around 65% of those with PDD having a history of CM (Wiersma et al., 2009). Furthermore, CM is linked to an earlier onset of depression, an increase in severity and chronicity of depression, and co-morbidity with other disorders (Nelson et al., 2017; Wiersma et al., 2009). Neglect and emotional abuse are thought to inhibit adaptive coping strategies developing, characterised by the "preoperational" cognitive development stage between the ages of 4 and 7 causing poor emotional control and a lower ability to tolerate distress (McCullough, 2000; Piaget, 1981). Research supports these factors are more commonly found in individuals with PDD than MDD (Barnhofer et al., 2014; Bird et al., 2018; Domes et al., 2016). McCullough (2000) suggests this happens through the triggering of early memories of shame and link to the development of dysfunctional cognitive patterns (Klein et al., 2009). Indeed, Guhn et al. (2018) found that autobiographical memories of difficult interpersonal experiences could be a factor in triggering dysfunctional coping in chronic depression. However, it is a mixed picture with recent reviews finding inconsistent support for CM being a moderating factor between chronic and non-chronic forms of depression (Köhler et al., 2019; Szpak, 2020). Furthermore, evidence suggests that CM could be a factor in reducing or stopping the response from psychotherapy (Baush et al., 2017; Nanni et al., 2012) implying there could be other more salient moderators in PDD.

2.2.2.2 Interpersonal difficulties

Findings suggest that interpersonal problems are an important aspect in the development and maintenance of depression, and it has been proposed that this is more pronounced in PDD (Leader & Klein, 1996; Bird et al., 2018). Interpersonal factors of hostility and submissiveness, as measured by the Interpersonal Inventory (IIP-32), were found to be linked to PDD (Constantino et al., 2008) while Constantino et al. (2012) found that the reduction in Hostile-Submissive interpersonal style was significantly related to decrease in depression scores through the clinician rated Impact Message Inventory (IMI). Two meta-analyses have found support for submissive and hostile

interpersonal styles as being a common factor for those with PDD (Bird et al., 2018; Köhler et al., 2019). Hostile, submissive and hostile-submissive (socially avoidant) interpersonal styles (Appendix C.) were found to be more pronounced in individuals with chronic depression compared with major depressive disorder (MDD) (Bird et al., 2018). However, these findings are tentative as research in this area is limited with few studies directly comparing chronic depression and MDD, and the quality of studies that do exist is poor (Bird et al., 2018).

2.2.3 Treating persistent depression

Treating early-onset PDD is thought to be challenging due to deep seated avoidance patterns in relating, which have been fostered by difficult childhood experiences resulting in ingrained unhelpful thoughts, feelings and behaviours (McCullough, 2020). Psychological interventions that have an evidence base for treating severe or persistent depression include CBT, Inter-personal psychotherapy (IPT), behavioural activation, and Cognitive Behavioural Analysis System of Psychotherapy (CBASP). These can be complemented with anti-depressant medication (The Matrix, 2015; National Institute for Health and Clinical Excellence (NICE), 2017). The European Psychiatric Association Guidance (EPAG) recommends combined treatment of pharmacotherapy and psychotherapy, with an interpersonal approach for the therapy (Jobst et al., 2015).

Anti-depressant medications (serotonin reuptake inhibitors (SRI's)) are routinely used in the treatment of depression, however, the rates of efficacy and remission using anti-depressants are unsatisfactory – in chronically depressed patients it is less than 30% (Ijaz et al., 2018; Krystal et al., 2011; Trivedi et al., 2006). Furthermore, issues with tolerating medication, common side effects and withdrawal are common, and this is made more difficult by the lack of appropriate alternative options such as therapy to support continued

improvement of depression symptoms and prevent relapse (Arnow et al., 2003; Kendrick, 2021; Saha et al., 2021). Some side effects of medication (e.g., sleep problems, sexual issues, eating) are questions on the depression questionnaires (BDI-II etc.) and may interfere with the true picture of depression symptoms (Hieronymus et al., 2021). Of note, a recent analysis of the Combining Medications to Enhance Depression Outcomes (CO-MED) trial found that those with PDD and CM did not respond differently to medication than those without CM, but the burden of side effects was more pronounced (Medeiros et al., 2021). Patient preference for psychological therapy has been demonstrated in McHugh et al. (2013) meta-analysis and meeting patient's choice for treatment has been shown to be a factor which can improve efficacy and reduce drop-out from treatment (Mergl et al., 2011; Swift et al., 2011; Williams et al., 2016).

Reduced social support may be a predisposing factor for the development of depression and can increase the likelihood of dropout from therapy due to lessened ability to navigate social functioning (Keller et al., 2014). Patient's with PDD often have co-morbid Axis I and II disorders, combined with traumatic childhoods, and may feel worthless and hopeless. This can make the therapeutic relationship challenging with the possibility of countertransference and strong emotional reactions, and in some cases a rupture or disengagement could happen (Klein & Santiago, 2003; McCullough, 2020). However, the evidence for treating PDD comes from clinical trials which often lack ecological validity, for example, in recruitment and by excluding participants with co-morbid disorders, and in reality, clinical practice is very different (Trivedi et al., 2006).

2.2.3.1 Cognitive Behavioural Analysis System of Psychotherapy (CBASP)

CBASP is the only model of psychotherapy specifically designed to treat PDD, and it aims to teach individuals to understand and modify their unhelpful contributions in interpersonal situations for a more positive or beneficial interaction (McCullough, 2020). It utilises cognitive, behavioural, psychodynamic and interpersonal techniques facilitated by a therapist who uses their own relationship with the person to model and facilitate change (McCullough, 2003). The model proposes that chronic depression is triggered by poor relational expectations due to CM and the persons interpersonal response isolates and maintains the depression leading to it developing early and becoming chronic (McCullough, 2000). McCullough (2020) depicts the patient with early on-set PDD as functioning with "cognitive-emotional maturity level of a 4–6-year-old child" (McCullough, 2020, p3).

2.2.3.1.1 Evidence base for CBASP

CBASP has a good evidence base for treating chronic depression (Furukawa et al., 2018; Keller et al., 2000; Kriston et al., 2014; Negt et al., 2016; Schramm et al., 2011; Wiersma et al., 2014) and is a recommended treatment for PDD in Europe and the United Kingdom (Jobst et al., 2015, The Matrix, 2015; NICE, 2017) though it is not commonly available in routine services (Schramm et al. 2017). CBASP was found to be moderately more efficacious than non-specific psychotherapy in an RCT of patients suffering from early-onset chronic depression, with remission rates of over 36% (Schramm et al. 2017). A re-analysis of this data has found that patients with moderate to severe depression and CM were more likely to respond to CBASP while those with less severe symptoms, better social functioning and quality of life responded better to supportive psychotherapy, giving some support to McCullough's (2003) theory of CM affecting interpersonal functioning (Serbanescu et al., 2020). However, this study may lack ecological validity as it only selected patients who were not on anti-depressant medication not reflecting the reality of everyday outpatient experience.

A recent analysis using individual patient data found evidence that a combination of anti-depressant medication and CBASP was more effective than either treatment alone with less likelihood of drop out from treatment (Furukawa et al. 2018). Using patient characteristics, it is suggested that treatment can be tailored for individuals, for instance co-morbid symptoms may mean CBASP alone is more suitable (Furukawa et al. 2018). However, a longer term follow up of CBASP suggests that for early-onset PDD patients 32 sessions over 48 weeks may not be enough dose for a long-term reduction of symptoms, with only 50% achieving remission after two years (Schramm et al., 2019). This adds weight to the need for offering booster sessions and ongoing maintenance, as McCullough (2020) highlights that change needs support to be maintained as the skills learnt fade over time. A re-analysis using multilevel modelling of Michalak et al. (2015) study comparing Mindfulness Based cognitive therapy (MBCT) and CBASP group therapy suggested that MBCT was more advantageous for "vindictive/self-centred/hostile dominant" interpersonal type while CBASP was better for "non-assertive" in treating chronically depressed individuals (Probst et al., 2020).

2.2.3.1.2 Support for key factors in CBASP treatment

Vivian & Salwen (2013) summarised the components of CBASP treatment and highlighted some evidence for its theoretical underpinnings. They compare the Situational Analysis (SA), in which behaviour is the main aspect linking thoughts and feelings to outcomes, to functional analysis which is used in Beck's (1987) CBT therapy (Paykel, 1987) with main difference being achieving the desired outcome is the goal for change. Santiago et al. (2005) found evidence to suggest that the SA process of problem-solving real situations was linked to better outcomes, even when the effect of therapeutic relationship was accounted for, and Klein et al. (2011) found improvement in interpersonal problem solving led to decrease in depression symptoms. Furthermore, there have been indications that learning SA techniques online

can have a preventative effect on the development of anxiety and depression in a sample of college students (Cukrowicz et al., 2007).

Improvements in depression symptoms are proposed to happen through interpersonal change. Inpatients receiving 12 weeks of CBASP were found to have reduction in interpersonal distress that was significantly linked to a decrease in depression symptoms, however, this was a naturalistic study with no control groups (Guhn et al., 2021a). Klein et al. (2020) recently used sequential mediation to re-examine Schramm et al. (2017) CBASP advantage over SP and linked it to improvement in therapeutic relationship due to the reduction in the IIP measure of Hostile-submissive. Blalock et al. (2008) found CBASP reduced depression symptoms through change in escape-avoidance coping style.

Research has pointed to the added benefits of group therapy including supporting interpersonal improvement, positive peer interaction, shared learning and modelling (Lewinsohn & Clarke, 1999, Morrison, 2001) and group CBT for depression has been found to be as acceptable and efficacious as individual therapy (Cuijpers et al., 2019). Group CBASP has been established to be as effective as individual therapy and can deliver some additional advantages such as cost effectiveness, opportunities for social connection, practice interpersonal change to improve social functionality leading to a decrease in interpersonal problems (Locke et al., 2016; Michalak et al., 2015; Sayegh et al., 2012; Sabaβ et al., 2018). However, not a great deal is known about the factors that mediate the effect specifically in group CBASP and it is important that group therapies are developed and evaluated to maximise utility and cost-effectiveness (Guhn et al., 2021b; Sayegh et al., 2012). Even more so as there can be problems with research evidence being operationalised into clinical practice with protocols not being followed and recommended maintenance therapy not being offered (Schindler et al., 2011; Riihimaki et al.,

2017). Qualitative information gathered from a recent study of inpatients with PDD receiving 24 weeks of individual and group therapy found patients self-reported improvements following CBASP were “increased social competence, self-confidence, self-reflection, interpersonal dynamic and optimism” (Guhn et al., 2021b, p.9). Furthermore, there was a slight advantage with group therapy over individual CBASP but this could be attributed to the higher “dose” of group element adding benefit and unspecific benefits of group treatment are also not understood (Guhn et al., 2021b).

2.2.3.1.3 Learning and skill acquisition in CBASP

There is a lack of understanding of what parts of therapy works best for PDD and why, with research on single moderators often giving contradictory results with very small effects, and confounding factors difficult to prise apart (Jobst et al., 2015; Kraemer, 2013). The mechanisms of change in group CBASP are not fully known, though it is suggested that learning acquisition precedes change in symptoms, and this is a unique part of CBASP (McCullough, 2020). McCullough (2000) theorises that by achieving the learning objectives in CBASP through the tasks, such as the SA, the patient would move from the pre-operational to the formal operations thinking and that this would lead to better relationships and reduce depressive symptoms and distress. Evidence has shown that outcomes tend to improve after the core phase of treatment for chronic depression is complete and this supports longer input and a maintenance phase approach (Arnow & Constantino, 2003).

A measure of skill acquisition (the Patient Performance Rating Scale (PPRF)) is used to assess a patient’s ability to successfully complete SA. Manber et al. (2003) found PPRF success at midpoint in therapy predicted a positive outcome in CBASP and that medication did not mediate this result. Moreover, Santiago et al. (2005) found that therapeutic alliance and PPRF scores were small and individual predictors of improvement in depression symptoms during

CBASP treatment. These findings suggests that medication is adding to any positive effect separately and not facilitating the interaction with the skill acquisition leading to change (Manber et al., 2003; Santiago et al., 2005). However, there are issues with the PPRF as a measure as it is therapist rated and may bring bias into scoring and an independent rating system would avoid that (Manber et al., 2003). Santiago et al. (2005) suggest growth curve analyses could help explore relationships between skill acquisition and depression outcome over time

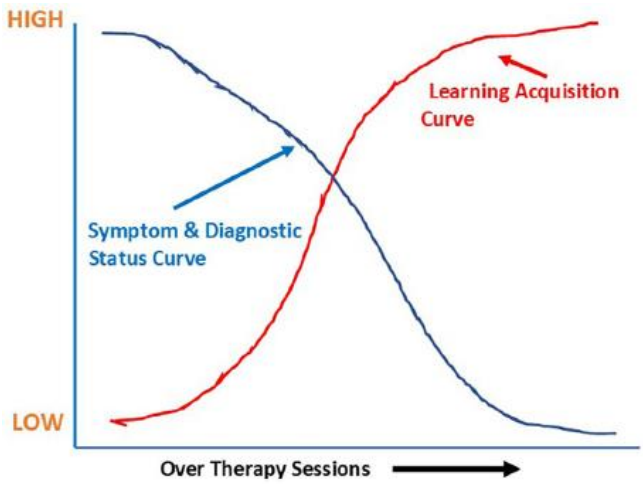


Figure 7. McCullough's (2020) "CBASP acquisition learning and symptoms assumption curves shown in a hypothetical design space".

The change in learning acquisition during CBASP is captured through two measures: The Personal Questionnaire – Situation Analysis (PQ-SA) and The Personal Questionnaire – Interpersonal Discrimination Exercise (PQ-IDE). McCullough (2020) described the change as the ability to achieve skills as measured by the PQ-SA and PQ-IDE increasing over time, while the depression symptoms decrease over time (Figure 7). Bird (2016) found in an analysis of Swan et al.'s (2013) single case series data a linear change in symptoms from individual CBASP.

The PQ-SA captures the patient's understanding of their interpersonal functioning ("perceived functionality"), and hostile and submissive personality traits, which were potentially adaptive when a person was experiencing CM, impinge on the development of meaningful relationships (McCullough et al., 2000). The PQ-SA measures the patient's understanding of the impact that their behaviour has on situations and desired outcomes (Bird et al., 2018; Köhler et al., 2019). The Personal Questionnaire – Interpersonal Discrimination Exercise (PQ-IDE) which measures feelings of interpersonal safeness in discriminating the therapist from significant others ("dyadic safety") (McCullough, 2020). The impact of CM, which is often interpersonal trauma, leads to poor emotional control, maladaptive coping and shame based dysfunctional thinking patterns (Barnhofer et al., 2014; Domes et al., 2016; Guhn et al., 2018; Klein et al., 2009; McCullough, 2000); this prevents the person feeling safe in interpersonal situations and the IDE process of supporting the person to discriminate the therapist, and then others out-with the sessions is the process of change. Being stuck in pre-operational thinking does not allow the patient to generalise previous positive interpersonal situations and the CBASP therapy environment cultivates and encourages this change to formal operations thinking (McCullough, 2000; Piaget, 1981).

2.2.4 Current study

With issues of implementing RCT's into clinical practice and added advantages of groups it is important to evaluate the efficacy and change processes in group treatment for PDD (Morrison, 2001; Riihimaki et al., 2017). Due to the COVID-19 pandemic restrictions prohibiting the ability to carry out novel research, a secondary dataset was sourced and utilised. A range of data was collected routinely by practitioners as part of CBASP treatment. The data was intended to be used to evaluate the efficacy of the intervention. The current study aimed to explore the process of change in a sample of persistently depressed patients who attended group CBASP in the community, by investigating if skill acquisition in CBASP was linked to a change in overall distress (CORE-10)

and self-rated Mood score. Those attending the group would be likely to have experienced CM, have reduced interpersonal functioning, and present with hostile and submissive traits (Barnhofer et al., 2014; Bird et al., 2018; Domes et al., 2016; Guhn et al., 2018; Klein et al., 2009; McCullough, 2000). Based on McCullough's (2000) theory of skill acquisition causing interpersonal change which leads to positive outcomes, it was hypothesised that any change in symptoms would occur later in therapy as this unfolds. As the patient learns the effect their behaviour has on impacting interpersonal situations by doing the SA, they try changing their behaviour and this would lead to improved functioning (as measured by the PQ-SA) and then reduced symptoms. Learning in the IDE would be hypothesised to change as a person feels safer in interpersonal situations, following from learning to discriminate the therapist from the SO, and applying this to other situations outside therapy, leading to improved discrimination (measured by PQ-IDE) and change in symptoms. As the thinking moves from pre-operational to formal operations thinking (McCullough, 2000; Piaget, 1981) the learning would be generalised. Change was investigated by fitting a multilevel model to the participants data to examine if it is linear or non-linear in nature. Measures of skill acquisition (PQ-SA, PQ-IDE, PPRF) were added to the model to explore their relationship to symptoms change. Furthermore, change in interpersonal functioning was reviewed using the IIP-32 with an expectation that there would be improvements in hostile/submissive domains. It is thought that the group element of CBASP might offer an advantage to individual therapy by facilitating interpersonal change through positive peer interaction, group role play and modelling (Guhn et al., 2021b; Locke et al., 2016; Sayegh et al., 2012).

It was predicted that there would be an increase in measures of learning acquisition of CBASP skills (PQ-SA, PQ-IDE, PPRF) that precedes the reduction of distress and depression symptoms over the time of the group and that this change will be non-linear (McCullough, 2000). In addition, it was thought that there would be a decrease in depression symptoms, overall

distress, and an increase in mood scores over the group. It was expected that patients and therapist would report global differences in symptoms. Change in interpersonal style were hypothesised in the hostile, submissive and hostile-submissive domains.

2.3 Methods

Ethical approval was granted by the University of Edinburgh and Caldicott. Confirmation was given that NHS ethics were not required (see Appendix E & F).

2.3.1 Participants

Individuals experiencing long-term depression symptoms were offered a CBASP group as treatment after being assessed in a psychological therapies primary care service in the UK. Eighty-six people opted in and were assigned to thirteen groups which ran consecutively from 2011 to 2021. Baseline and outcome data was collected routinely in the service. This study was registered with Open Science Framework (OSF) (osf.io/4cthz).

2.3.2 Measures

Routine measures were collected throughout and are detailed below:

Clinical Outcomes in Routine Evaluation Outcome Measure (CORE-OM) (Evans et al., 2002) and Clinical Outcomes in Routine Evaluation 10 (CORE-10) (Barkham et al., 2013). A self-report measure of overall psychological distress, including anxiety, depression, trauma and risk questions, giving a score out of 40. This measure has good reliability, validity and is sensitive to change.

Beck Depression Inventory – Second Edition (BDI-II) (Beck et al., 1996). A self-report 21 item measure of depression, using score or 0-3 to measure occurrence and severity of symptoms. It is reliable and valid with good internal consistency (Beck et al., 1996).

Inventory of Interpersonal Problems – 32 (IIP-32) (Horowitz et al., 2000). A 32 item self-report measure to examine interpersonal issues and related distress. It has eight scales with good agreement and is sensitive to measuring change.

Patient Global Impression - Improvement scale (PGI), Clinical Global Impression – Improvement (CGI-I) and Clinical Global Impressions – Severity (CGI-S) (Guy, 1976). These are general measures of severity and treatment response commonly used in UK primary care mental health services. PGI is a 7-point scale (1= very much improved, 7 = very much worse) of patient rated global functioning. CGI-I is the clinician rated improvement score on the same scale. The CGI-S is the clinician rated severity scale (1 = Normal, not at all ill to 7 = Among the most extremely ill patients). These measures are valid for use for patients with major depression with concordance between PGI and CGI (Mohebbi et al., 2018).

Specific CBASP measures collected in line with CBASP manual guidelines during the therapy sessions (McCullough, 2006). They include:

Personal Questionnaire – Situation Analysis (PQ-SA) (McCullough, 2006). This is used to measure interpersonal perceived functionality and was collected at 5 points during therapy.

Personal Questionnaire – Interpersonal Discrimination Exercise (PQ-IDE) (McCullough, 2006). This is used to measure emotional discrimination learning and was collected 5 times over therapy in line with the CBASP manual guidelines.

Patient Performance Rating Scale (PPRF) (McCullough, 2000). The CBASP-G PPRF was adapted from the McCullough (2000) manual to 10

questions and is used to measure the client's competence at completing the situational analysis sections.

Additionally, a Mood score out of ten (ten being the best mood, one being the lowest) was taken every week at the start of the group for each participant as a measure of what their average mood was in the past week.

2.3.3 Procedure

Following an initial assessment at a psychological therapies service, patients deemed suitable with PDD symptoms were invited to attend a CBASP group. After opting in, each person attended three individual sessions with one of the therapists from the group. At these sessions baseline measures were completed (BDI-II, IIP-32, CORE-10). In addition, the Significant Other History (SOH) was completed for each patient. Each group consisted of twenty weekly sessions of 2 hours, and thirteen groups with 86 people invited to attend, running consecutively. The group followed the CBASP protocol (Appendix D.), and participants completed Situational Analysis (SA) and Interpersonal Discrimination Exercises (IDE), alongside the respective learning acquisition measures (PQ-SA, PQ-IDE) during the group. The PPRF was scored by the therapists over the course of the group by assessing the patient's SA's. BDI-II and IIP-32 were completed halfway through (week 10) and end of therapy (week 20). CORE-OM scores were taken at start and end of therapy in first three groups then weekly in groups four to thirteen. Mood scores (10 being best mood, 1 lowest) were taken at every week in groups two to thirteen. PGI, CGI-S and CGI-I were taken weekly from group five to thirteen.

2.3.4 CBASP-G Intervention

The group version of CBASP (CBASP-G) was developed to follow the core principles of individualised CBASP. Dr James P. McCullough, Jr developed CBASP spurred by his reflections of his clinical experience of working with

long-term depressed patients, who did not respond as well to traditional treatments such as CBT (McCullough, 2000). The theory underlying CBASP suggests that children who experience maltreatment may develop adaptive ways of coping (e.g., avoiding the threat or being submissive) and result in an expectation that other relationships will be the same, which would maintain fear and avoidance in interpersonal interactions. McCullough (2000) states that these early experiences leave the person “like a wounded child” in their adult relationships where they expect others to cause them harm if given the chance. McCullough (2000) links this difficulty in chronically depressed individual’s to being emotionally “stuck” in Piaget’s (1981) “pre-operational” stage of development (Piaget, 1981). The expectation that others will have bad intentions (like the significant other that maltreated) makes it hard for the individual to build trusting relationships. This could result in early onset depression which is typical of those with chronic types of depression (McCullough, 2000). In late onset chronic forms of depression people are theorised to have a deterioration in cognitive emotional functioning due to a significant negative event that leaves the person helpless and hopeless about their situation improving (McCullough, 2000).

The CBASP model uses cognitive, behavioural and interpersonal techniques to allow the patient to reflect on how they interact with others and try doing things differently to aim to get their needs met. The process in CBASP of examining unhelpful interpersonal patterns and actively working to foster adjustment in interpersonal situations is theorised to offer change in interpersonal approach and reduce depression. This is facilitated by the therapist who uses a Disciplined Personal Involvement (DPI) approach to model and encourage interpersonal change (McCullough, 2003). This is traditionally a highly unusual role for therapists to take as in CBASP they use their personal feelings and thoughts in a specific and controlled manner to expedite change in the patient, and such personal input is usually forbidden in other therapy modalities (McCullough, 2006 & 2020). McCullough (2020)

states that PDD is a “lifetime disorder” that can be managed by practicing CBASP skills and maintenance support can ensure this is continued.

Patients attended three individual sessions with a group therapist to collect baseline measures, complete a timeline, and develop a Significant Other History (SOH), which involves identifying key people who have influenced how they think and behave and interact interpersonally, and reveals key interpersonal fears (McCullough, 2020). From the SOH a transference hypothesis (TH) was created to help conceptualise the predicted fearful expectations of how others in the group and the therapists will react negatively towards them (McCullough et al., 2006). The group element of the intervention is run from the CBASP-G protocol (Appendix D.). The first session consists of psychoeducation around persistent depression and CBASP, and the setting of group ground rules. Each person is required to introduce themselves and give “hopes and fears” of coming to the group. Filling in the first PQ-SA is a task of the first session, and this requires the participant to mark along a line-scale of 0 to 10 how their current thinking answers if they see a connection between their behaviours and how things turn out for them on a line scale from No (0) to Yes (10). At the second session, previous completers of CBASP-G share their experience, previous learning is shared (Transference Hypothesis (TH)), discussion about the importance of their current interpersonal relationships, and the Situational Analysis (SA) is introduced. PQ-IDE is filled in to measure in similar method to PQ-SA to measure how well the individual can discriminate between maltreating interpersonal relationships and therapist/group member using the TH.

The following sessions are a combination of group exercises, discussions, role play using the SA as a learning tool. The SA is completed by the participant weekly as homework using interpersonal issues that arise, in session they are reviewed together and the therapists complete the PPRF after the session

giving a rating out of 100% of how well the learning in the SA has been demonstrated. At each weekly session the group members fill out CORE-10, PGI, and therapists fill in the CGI-I and CGI-S, and a self-reported Mood rating is taken. The PQ-SA is completed at groups 5, 9, 13 and 17 and the PQ-IDE at 7, 11, 15, and 19. The question in the PQ-IDE was changed in Group 8 from discriminating others in group from SO to adding a rating of others more generally. An interpersonal discrimination exercise (IDE) is introduced at session 10 to work on a situation which the recalled behaviours of a SO maladaptive interpersonal relationship can be contrasted with how the therapist responds to the same situation. The IDE therapy procedure takes place throughout group therapy when the opportunity arises, and the PQ-IDE and PQ-SA are collected regularly to assess learning acquisition of the skills. The main content of CBASP-G is the evaluation of the SA and IDE homework and using that to inform role-play, discussions and exercises to facilitate interpersonal learning.

2.3.5 Data preparation

Data was extracted from questionnaires into an excel file. Where more than one PPRF was collected for a week, the scores were averaged. Unfortunately, there was a sizeable amount of data missing or unavailable from the secondary dataset. Of the 80 participants who started treatment only 30 had CORE-10 at start and finish and only 26 BDI-II scores at both. This was not only due to non-attendance – in some cases the start data was unavailable or not accessible to the research team. The available data that was collected weekly (CORE-10 and Mood) was around 60% that could be used in the MLM analysis.

2.3.6 Data Analysis

Data analysis was performed using IBM SPSS for Macintosh (Version 25) (2017). Since, the outcome measures were routinely collected in clinical practice there were multiple data points missing. Six participants who did not

start the group were removed from the analysis, leaving 80 participants providing some data. See participant flow and data collection diagram (Figure 1.).

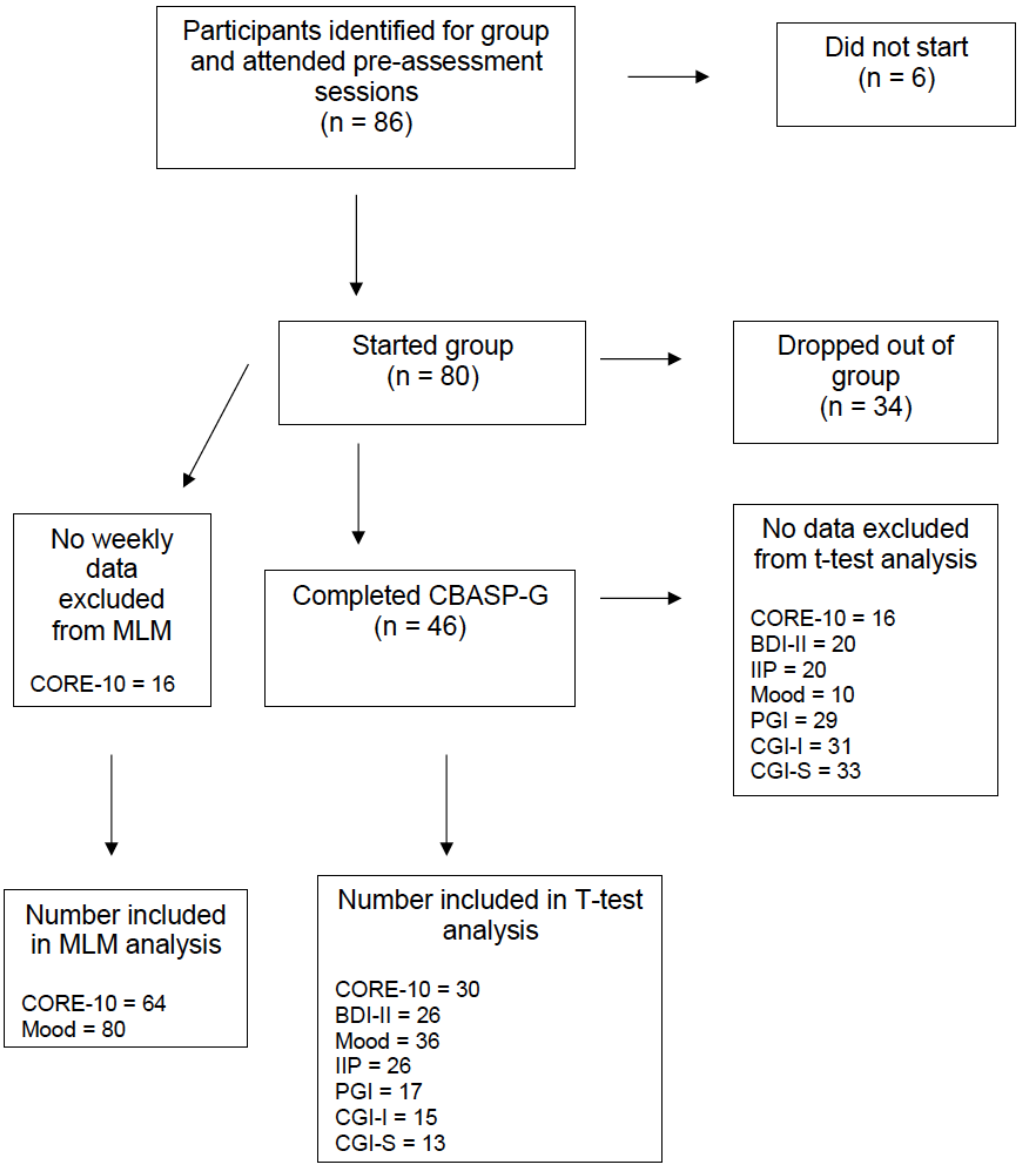


Figure 8. Diagram of participant flow and data collection.

2.3.6.1 Paired t-tests

Paired t-tests were carried out on the main outcome measures to examine overall effectiveness of the intervention (BDI (start to finish/week 20), CORE-10 score (week 1 to week 20), Mood rating (week 1 to week 20) and IIP (start to week 20 total, hostile, submissive and hostile submissive) and PGI, CGI-S and CGI-I (week 1 to week 20)). The t-tests were run for participants that had data for both time points (Actual) (Table 1.) and regression imputation (Multiple Imputation) methods were carried out to handle the missing outcome data. Multiple imputation was chosen as the most appropriate way to handle the missing data, since it was missing at random, and t-tests were re-run with data imputed by this method (Jakobsen et al., 2017).

2.3.6.2 Multi-level Modelling

A Multi-level modelling statistical method (MLM) was selected to investigate patterns of change in Mood and CORE-10 score and if change was linked to the acquisition of learning CBASP skills. There were three levels of data: weekly scores at time points (Level 1), which are nested in individuals (Level 2) and they are nested in the group that was attended (Level 3) (Field, 2013). MLM is advantageous as it can model variance of regression slopes, can model relationships between residuals and due to the nature of this real-life clinical data sample it can maximise the data as MLM does not require complete data sets and can handle missing data well (Field, 2013).

The weekly collected data included CORE-10, Mood rating, PPRF score, PGI, CGI-I and CGI-S. This data was restructured to time point for analysis in SPSS and initially visually checked for equality of variance. Weekly data collection for CORE-10 was not started until Group 4 and the Mood ratings until Group 2, therefore, since the missing data was not random the analysis was run for the Mood data Groups 2 to 13 and the CORE-10 groups 4 to 13 (Jakobsen et al., 2017). Data was checked to see which growth model was most suitable for

the dependent variable (CORE-10 and Mood); linear, quadratic and cubic trends were modelled. The intraclass correlation (ICC) was calculated to see how much variability in the outcome is attributable to each level (group, individual) using the calculation: ICC = (intercept variance/(intercept variance/residual)) (Field, 2013). The -2 Restricted Log Likelihood (-2LL) was checked to assess if the chi-squared difference between each model was significant.

Several models were created and the data for weekly CORE-10 and Mood measures used:

Model 1 – An unconditional model was set up with no predictors but allowing the intercept term to vary to calculate which proportion of variance is between participants. The covariance parameter estimates were used to calculate the ICC – variance between participants.

Model 2 – Unconditional linear growth model was set up with the time-point variable to fit the model for change over time for the whole sample with random intercepts and check the trend of scores over time.

Model 3 – Unconditional linear growth model allowing slope variation was set up, by adding Time to the random effects. This was to check if people have different rates of change.

Model 4 – Model of the correlation structure of within (repeated) measures effects which are likely to be non-independent (e.g., one measure week 1 is likely to be more similar to week 2 measure than week 20 measure). An autoregressive structure was used to model this.

Model 4a – The model was adjusted to test for level 3 (group) effects to see if time was significant for each group.

Model 5 – The model was adjusted to add in fixed effect and test for interaction effect, to test for change in relation to the CORE-10 or Mood change. Measures of learning acquisition (PPRF, PQ-SA, PQ-IDE) were added into the

model one at a time to attempt to explain the difference in growth and assess for fit. This was performed for IIP-32 values, BDI-II, CGI-I, CGI-S and PGI too.

2.4 Results

2.4.1 Sample characteristics

The age range of participants was 20 to 64 years old and a mean (SD) of 43.02 (10.07) years. There were 61.6% female participants (53 female to 33 male). Mean (SD) number of sessions attended was 13.05 (6.02). Baseline measures mean (SD) were CORE-10 18.90 (7.52) and BDI-II 30.86 (11.59). Drop-out from the group was 42.5%.

2.4.2 Paired T-tests results

Paired t-tests are reported in Table 4.

2.4.2.1 CORE scores

CORE-10 was compared from pre-group to week 1 and data was normally distributed with no outliers. The paired t-test showed that the small difference from CORE pre to CORE week 1 was non-significant (0.667 (1.751) $t(5)$=0.933, p=0.394 . Therefore, since there were only some CORE pre data which was likely not missing at random, CORE week 1 was used for analysis. A paired samples t-test was performed to see if there was a statistically significant mean difference between CORE-10 score from week 1 to week 20 (end of group) (see Table 1.). Data are mean (standard deviation (SD)), unless otherwise stated. No outliers were detected as assessed by boxplot inspection. The assumption of normality was assessed using Shapiro-Wilk's test

(*p*=0.262). The CBASP group elicited a statistically significant decrease in CORE-10 score from week 1 (19.33 (7.126) to week 20 (15.40 (7.833)) of 3.933 (95% CI, 1.282, 6.584), *t*(29)=3.034, *p*=0.005, giving a medium effect size of *d*=0.554.

2.4.2.2 Mood scores

Mood week 1 to week 20 was compared in a paired t-test. There was normal distribution and no outliers in the data. Of the 36 participants who had data for Mood the CBASP group elicited a statistically significant increase in Mood score from week 1 (5.014 (1.533) to week 20 (6.278 (1.775)) of -1.264 (95% CI, 1.282, 6.584), *t*(35)= -3.768, *p*=0.001, giving a medium to large effect size of *d*=-0.628.

2.4.2.3 BDI-II

Of 41 people who provided a BDI-II score at the end of therapy, 12 had reached remission (BDI-II<10). There was a statistically significant decrease in BDI-II scores from the start of therapy (30.04 (10.623) to finish (19.81 (12.737) of 10.231 (12.478) (95%CI, 5.191, 15.271), *t*(25)=4.181, *p*<0.001), giving a large effect size of *d*=0.820.

Table 3. Paired T-test scores

	Paired T-test Scores	
	Actual	**Multiple Imputation**
BDI-II (mean (SD) scores)	N = 26	N = 79
Baseline	30.04 (10.623)	33.41 (8.650)
End of therapy	19.81 (12.737)	20.29 (11.797)
t (df), p-value, Cohen's *d*	4.181 (25), $p < 0.001$, $d = 0.820$	10.991 (78), $p < 0.001$, $d = 1.237$
CORE week 1 to 20 (mean (SD) scores)	N = 30	N = 73
Week 1	19.33 (7.126)	20.38
Week 20 (End of therapy)	15.40 (7.833)	14.19
t (df), p-value, Cohen's *d*	3.034 (29), $p = 0.005$, $d = 0.554$	5.958 (72), $p < 0.001$, $d = 0.591$
IIP total (mean (SD) scores)	N = 26	N = 79
Baseline	14.104 (3.894)	15.1067 (3.206)
End of therapy	12.504 (5.318)	12.090 (3.531)
t (d.f.) *p-value,* Cohen's *d*	1.805 (25), $p = 0.083$, $d = 0.354$	7.024 (78), $p < 0.001$, $d = 0.790$
IIP – Hostile submissive (mean (SD) scores)	N = 26	N = 79
Baseline	2.558 (0.928)	2.575 (0.933)
End of therapy	1.731 (0.954)	2.051 (0.867)
t (d.f.) *p-value,* Cohen's *d*	3.433 (25) $p = 0.002$, $d = 0.673$	3.888 (78), $p < 0.001$, $d = 0.437$
IIP – Hostile (mean (SD) scores)	N = 26	N = 79
Baseline	1.937 (0.929)	2.030 (0.914)
End of therapy	1.731 (0.954)	1.565 (0.873)
t (d.f.) *p-value,* Cohen's *d*	1.617 (25) $p = 0.118$, $d = 0.317$	3.762 (78) $p < 0.001$, $d = 0.423$
IIP – Submissive (mean (SD) scores)	N = 26	N = 79
Baseline	2.521 (0.780)	2.603 (0.851)
End of therapy	2.192 (1.028)	2.019 (1.002)
t (d.f.) *p-value,* Cohen's *d*	1.731 (25) $p = 0.096$, $d = 0.340$	4.686 (78), $p < 0.001$, $d = 0.527$
Mood (mean (SD)) scores	N = 36	N = 67
Week 1	5.014 (1.533)	4.704 (1.619)
Week 20 (End of therapy)	6.278 (1.775)	6.144 (1.612)
t (d.f.), *p-value,* Cohen's *d*	-3.768 (35), $p = 0.001$, $d = -0.628$	-6.283 (66), $p < 0.001$, $d = -0.693$

2.4.2.4 IIP-32 score

A paired samples t-test was performed to see if there was a statistically significant mean difference between IIP-32 total, hostile, submissive and hostile submissive score from start to finish. Data are mean (SD), unless otherwise stated. No outliers were detected as assessed by boxplot inspection. The assumption of normality was reached using Shapiro-Wilk's test. The CBASP group elicited a non-statistically significant decrease in IIP-32 total score of 1.60 (95% CI, -0.22577, 3.42577), $t(25)=1.805$, $p=0.083$. Similarly, there was a small reduction but not reaching significance for hostile IIP score ($p=0.118$) and submissive IIP-32 score ($p = 0.096$). However, for hostile submissive IIP there was a significant reduction ($t(25)=3.433$, $p=0.002$). IIP

Hostile-submissive had one outlier (participant 41), which was a true value. A re-run of the t-test after removing the outlier saw a smaller reduction of 0.400 (95% CI, 0.042, 0.758), $t(24)=2.307$, $p=0.030$, and the effect size dropped to medium $d=0.461$.

2.4.2.5 PGI, CGI-I and CGI-S

PGI, CGI-I and CGI-S were checked for normality and due to the categorical nature of the data and it potentially being skewed towards scores of 2 and 3 (min and much improved) PGI, CGI-I and CGI-S were all not normally distributed (data are medians unless otherwise stated). PGI also had an outlier (60) but since this was a true value, this was kept in the analysis. Due to the spread of data not being symmetrical and there being an outlier, a non-parametric sign-test was used. An exact sign test was used as there were fewer than 25 values (Laerd statistics, 2021). In total, of the 17 participants,12 had improvements in PGI, while 5 had no difference. There was a statistically median decrease (improvement) in PGI (1 level) from week 1 (4) to finish (3), $p<0.001$ (Table 5.).

CGI-I had 15 participants and 15 had improvements in CGI-I. There was a statistically median decrease (improvement) in CGI-I (2) from week 1 (4) to finish (2), $p<0.001$. CGI-S had 17 participants (data are medians unless otherwise stated) 15 had improvements in CGI-S and 2 had no change. There was a statistically median decrease (improvement) in CGI-S (2) from week 1 (4) to finish (3), $p<0.001$.

Table 4. Exact sign test scores.

	Scores exact sign test
	Actual
PGI week 1 to week 20 (median scores)	N = 17 Improved = 12 Not improved = 0 Ties = 5
Result	
Week 1	4
Week 20	3
Diff in PGI	1
p-value	$p < 0.001$
CGI-I week 1 to week 20 (median scores)	N = 15 Improved = 15 Not improved = 0 Ties = 0
Week 1	4
Week 20	2
Diff in CGI-I	2
p-value	$p < 0.001$
CGI-S week 1 to week 20 (median (SD) scores)	N = 17 Improved = 15 Not improved = 0 Ties = 2
Week 1	4
Week 20	3
Diff CGI-I	2
p-value	$p < 0.001$

2.4.3 Multi-level modelling results

2.4.3.1 Modelling the change

Preliminary analyses were run for the CORE and Mood scores to check they were normally distributed. Model fit was examined using CORE scores and Mood scores (separately) and Time (linear), then adding quadratic ($Time^2$) and cubic trend ($Time^3$). Adding these did not improve the fit significantly so both CORE and Mood change are best described as linear, therefore, the subsequent models used a linear fit (Figures 9 & 10).

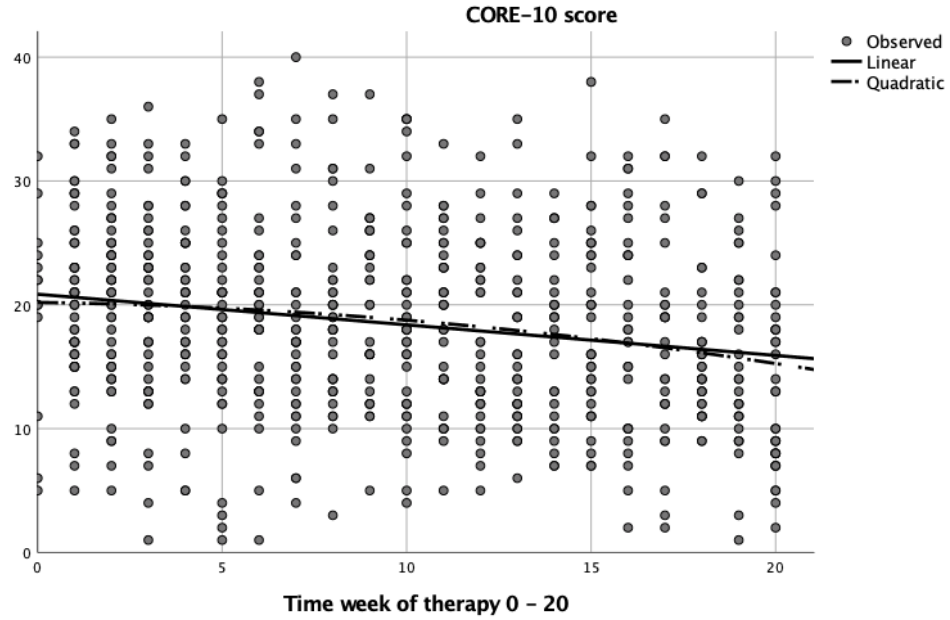


Figure 9. CORE-10 Linear fit

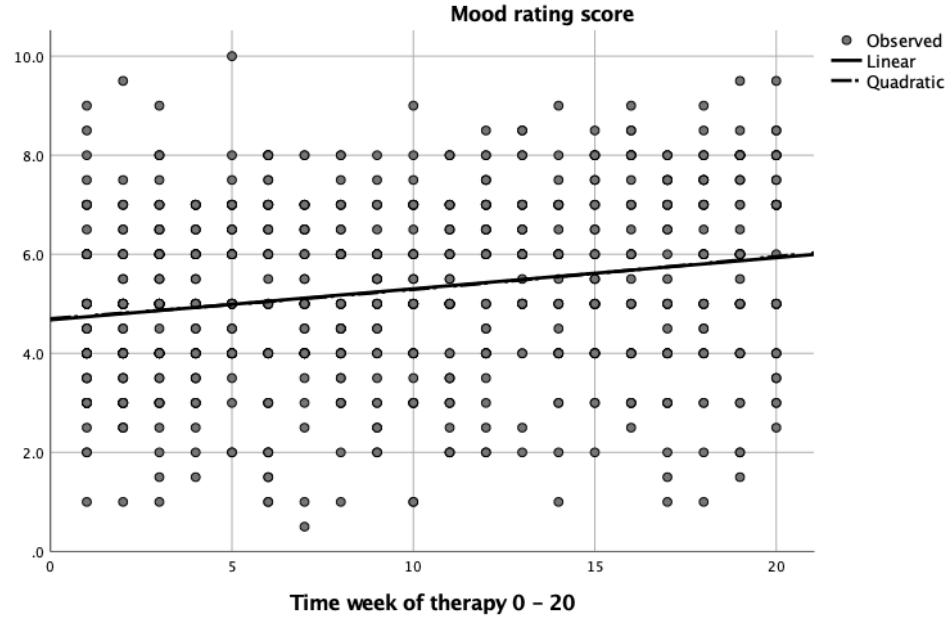


Figure 10. Mood Linear fit

2.4.3.2 CORE and Mood Multi Level Modelling

2.4.3.2.1 Unconditional model (Model 1)

This model was set up and run with no predictors to allow the intercept to vary by participant to assess the ICC(1), or proportion of the variance which is at the level 2 (participant level). CORE ICC(1)=0.644 and Mood ICCI(1)=0.439 indicating a substantial variance is attributable between participants for both. Furthermore, the variance term for the intercept is significantly greater than 0 (CORE 39.230 (7.950), $p<0.001$, Mood 1.351 (0.265), $p<0.001$ (see Table 6 and Table 7.).

2.4.3.2.2 Unconditional linear growth model (Model 2)

The time-point variable TIME was introduced to fit the model for change over time for the whole sample with random intercepts. Adding time into the model improves the fit for both CORE and Mood (-2LL reduced to 4355.738 and 3038.194 respectively). The fixed effect of TIME is negative and highly significant for CORE (-0.1823 (0.059), $p=0.003$), therefore, participants are lowering their CORE-10 score over time. The fixed effect of TIME is positive and highly significant for Mood (0.057 (0.008), $p<0.001$), with participants increasing mood score over the time in the group.

2.4.3.2.3 The unconditional linear growth model (allowing slope variation, Model 3)

TIME was added to the random effects in this model to investigate if individuals experience change differently. There was a significant improvement in model fit by allowing variation of intercepts with the -2LL reduced in the CORE model from 4355.738 to 4288.986 and Mood model from 3038.194 to 3013.159. There was a significant variation of the intercepts suggesting there is a spread of CORE-10 and Mood scores at the beginning and that individuals are starting from different points. The variation in the growth model between participants (slope variation term (UN(2,2)) is significant CORE $\beta=0.121$ (0.036), $z=3.356$

(0.067, 0.217), *p*=0.001; Mood β=0.003 (0.001), *z*=2.674 (0.002, 0.007), *p*=0.007, suggesting people are improving at different rates. The co-variance between slope and intercept is non-significant for both (CORE *p*=0.222, Mood *p*=0.922), suggesting there does not appear to be a relationship between someone's initial score and their likelihood to experience change in CORE-10 or Mood score. Furthermore, the fixed effect of TIME is still significant (CORE p=0.003; Mood p<0.001), therefore, the CORE-10 is reducing, and Mood score is increasing, over time with rates of change varying between individuals.

2.4.3.2.4 Within-subjects variance autoregressive structure (Model 4)

Within-subject variance was added to the model using an autoregressive structure to account for the corelation structure of within subject's effects for the repeated measures scores, as these are likely to be non-independent, accounting for nuisance variance (Beaumont, 2012). This improved the fit further reducing the -2LL significantly for CORE 4235.700 and Mood 3000.946 and the rho parameter was significant (CORE β=0.363 (0.049), *z*=2.446 (0.036, 0.180), *p*<0.001; Mood β=0.003 (0.001), *z*=1.959 (0.001, 0.007), *p*=0.001) indicating there is a positive relationship in adjacent time points.

2.4.3.2.5 Fixed effect of Group (Model 4a)

The effect of CBASP-G was considered by fitting the Group number attended to the multilevel model and comparing the results with other CBASP studies (inpatient and individual modalities of treatment) (Guhn et al., 2021b; Swan et al., 2013). The level 3 factor of group the participant attended was introduced into the model. In the CORE model Group*TIME had a significant effect (p=0.003) and closer inspection the significance was from one group – Group 9. Removing Group 9 kept the fixed effect of Group*Time significant but there were no groups showing significance. For the Mood model, full iteration was not achieved so the result was not reliable, as the validity of the model fit was uncertain.

2.4.3.2.6 Adding PPRF, PQ-SA, PQ-IDE to explain growth (Model 5)

Next, the learning acquisition co-variates (PPRF, PQ-SA, PQ-IDE) were introduced into the model to investigate if competence in achieving this skill explained any difference in the growth models. Adding PPRF and PQ-IDE reduced the -2LL significantly, improving the model fit but the co-variants either alone or by TIME were not significant. Adding PQ-SA also gave a significant reduction in -2LL of CORE to 1113.452 and Mood to 777.903 and PQ-SA had a significant effect β=-0.575 (0.246), (*p*=0.021) in the CORE model and PQSA*Time had a significant effect β=0.012 (0.005), (*p*=0.022), though the fixed effect of Time became non-significant for both. IIP was added to the model but the iteration did not fully run, therefore, the model data was not reliable and are not reported. There may have been insufficient data since there was only 3 out of 21 timepoints at maximum available for each participant.

Growth curve modelling was carried out to examine if the growth in skill acquisition measure was different to CORE and Mood linear change. PQ-SA was found to have quadratic change F(1,169.730) = 10.138, *p*=0.002 (Figure 11).

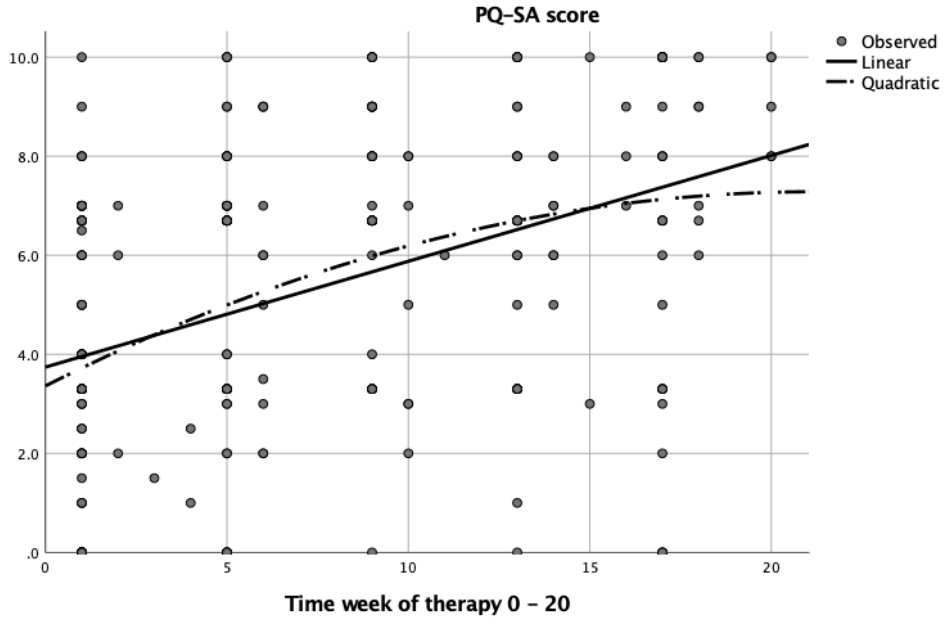


Figure 11. PQ-SA curve fit graph.

PQ-IDE was also found to have quadratic change F(1,160.198)=10.291, *p*=0.002 (Figure 12.).

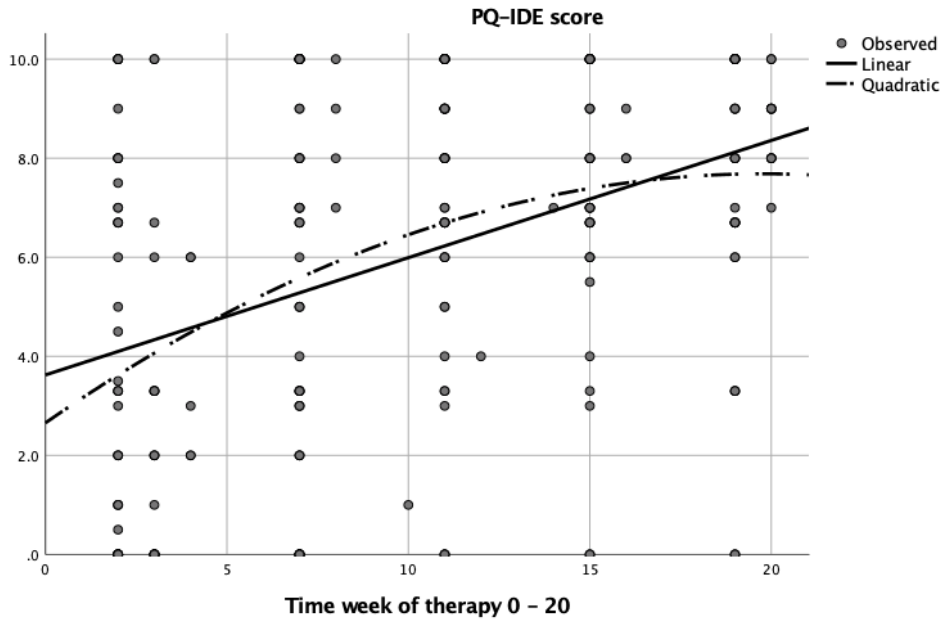


Figure 12. PQ-IDE curve fit graph

PPRF was found to have quadratic fit F(1,496.416)=8.605, *p*=0.004 (Figure 13.)

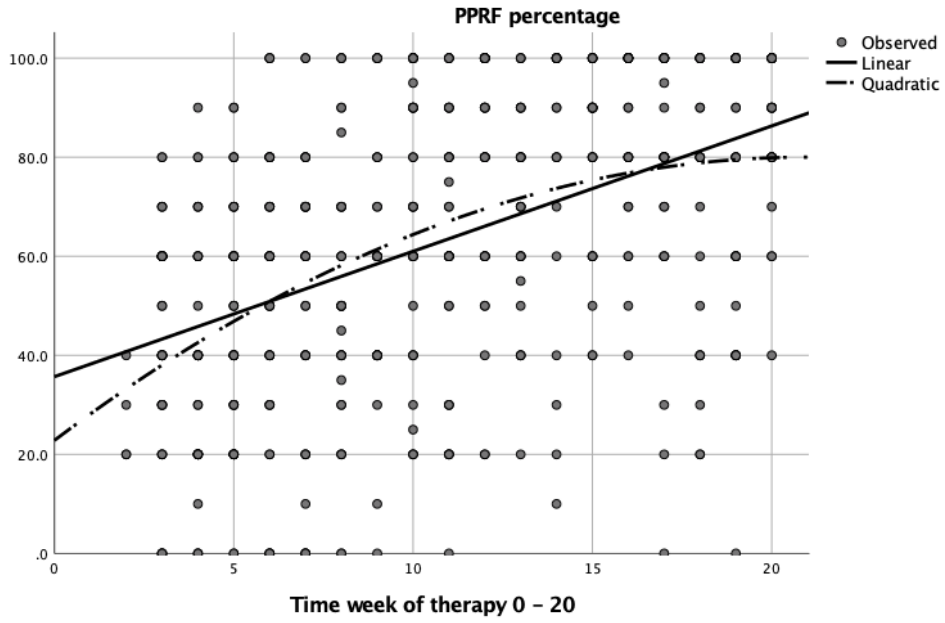


Figure 13. PPRF curve fit graph

Table 5. CORE-10 Multi-level modelling results

		CORE MLM results					
Model	**Description**						
1. Unconditional model	**Fixed effect**	**β/Estimate (SE)**	***t***	***p*-value**	**-2LL**	**ICC**	
	Intercept	19.263 (0.844)	22.833	*p*<0.001	4385.517	0.644	
	Variance	**β/Estimate (SE)**	***z***	***p*-value**			
	Residual	21.675 (1.201)	18.052	*p*<0.001			
	Intercept	39.230 (7.950)	4.934	*p*<0.001			
2. Unconditional linear growth model	**Fixed effect**	**β/Estimate (SE)**	***t***	***p*-value**	**-2LL**	**ICC**	**χ^2 diff, (Model 2-1) *p*-value**
	Intercept	20.710 (0.852)	24.359	*p*<0.001	4355.738	0.640	29.779, *p*<0.01
	Time	-0.1823 (0.059)	-3.123	*p*=0.003			
	Variance	**β/Estimate (SE)**	***z***	***p*-value**			
	Residual	20.697 (1.147)	18.044	*p*<0.001			
	Intercept	36.72 (7.427)	4.944	*p*<0.001			
3. Unconditional linear growth model (allowing slope variation)	**Fixed effect**	**β/Estimate (SE)**	***t***	***p*-value**	**-2LL**	**ICC**	**χ^2 diff, (Model 3-2) *p*-value**
	Intercept	20.782 (0.853)	24.539	*p*<0.001	4288.986	0.690	66.752, *p*<0.01
	Time	-0.1828 (0.585)	-3.123	*p*=0.003			
	Variance	**β/Estimate (SE)**	***z***	***p*-value**			
	Residual	16.911 (0.976)	17.325	*p*<0.001			
	Intercept (+ TIME)	37.72 (8.005)	4.712	*p*<0.001			
4. Add within-subjects variance autoregressive structure	**Fixed effect**	**β/Estimate (SE)**	***t***	***p*-value**	**-2LL**	**ICC**	**χ^2 diff, (Model 4-3) *p*-value**
	Intercept	20.820 (0.851)	24.477	*p*<0.001	4235.7	0.637	53.286, *p*<0.01
	Time	-0.194 (0.056)	-3.453	*p*=0.001			
	Variance	**β/Estimate (SE)**	***z***	***p*-value**			
	AR1 diagonal Residual	19.193 (1.465)	13.105	*p*<0.001			
	Intercept (+ TIME)	33.653 (8.035)	4.189	*p*<0.001			
4a. Adding fixed effect of group	**Fixed effect**	**β/Estimate (SE)**	***t***	***p*-value**	**-2LL**	**ICC**	**χ^2 diff, (Model 4a-4) *p*-value**
	Intercept	18.489 (3.850)	4.820	*p*<0.001	4170.881	0.638	64.819, *p*<0.01
	Time	-0.142 (0.206)	-0.690	*p*=0.496			
	Variance	**β/Estimate (SE)**	***z***	***p*-value**			
	AR1 diagonal Residual	18.943 (1.420)	13.340	*p*<0.001			
	Intercept (+ TIME)	33.373 (8.839)	3.776	*p*<0.001			

Table 6. continued.

5a. Adding PPRF to explain growth	**Fixed effect**	**β/Estimate (SE)**	***t***	***p*-value**	**-2LL**	**ICC**	**χ^2 diff, (Model 5a-4) *p*-value**
	Intercept	20.320 (1.904)	10.672	*p*<0.001	1777.409	0.756	2458.291, *p*<0.01
	Time	-0.081 (0.177)	-0.459	*p*=0.647			
	PPRF	0.000 (0.025)	0.004	*p*=0.997			
	PPRF*TIME	-0.001 (0.002)	-0.620	*p*=0.536			
	Variance	**β/Estimate (SE)**	***z***	***p*-value**			
	AR1 diagonal Residual	14.519 (1.569)	9.256	p<0.001			
	Intercept (+ TIME)	45.001 (14.000)	3.215	0.001			
5b. Adding PQSA to explain growth	**Fixed effect**	**β/Estimate (SE)**	***t***	***p*-value**	**-2LL**	**ICC**	**χ^2 diff, (Model 5b-4) *p*-value**
	Intercept	22.816 (1.466)	15.558	*p*<0.001	1113.452	0.666	3122.248, *p*<0.01
	Time	0.142 (0.165)	0.861	*p*=0.392			
	PQSA	-0.575 (0.246)	-2..338	*p*=0.021			
	PQSA*TIME	-0.032 (0.024)	-1.325	*p*=0.189			
	Variance	**β/Estimate (SE)**	***z***	***p*-value**			
	AR1 diagonal Residual	16.37 (2.518)	6.501	*p*<0.001			
	Intercept (+ TIME)	32.594 (9.403)	3.466	*p*=0.001			
5c. Adding PQIDE to explain growth	**Fixed effect**	**β/Estimate (SE)**	***t***	***p*-value**	**-2LL**	**ICC**	**χ^2 diff, (Model 5c-4) *p*-value**
	Intercept	21.166 (1.558)	13.590	*p*<0.001	1090.481	0.709	3080.4, *p*<0.01
	Time	-0.122 (0.168)	-0.726	*p*=0.471			
	PQIDE	-0.136 (0.228)	-0.599	*p*=0.550			
	PQIDE*TIME	-0.003 (0.231)	-0.142	*p*=0.887			
	Variance	**β/Estimate (SE)**	***z***	***p*-value**			
	AR1 diagonal Residual	16.569 (3.189)	5.196	*p*<0.001			
	Intercept (+ TIME)	40.471 (12.665)	3.195	*p*=0.001			

Table 6. Mood score Multi-Level Modelling results

		Mood MLM results					
Model	**Description**						
1. Unconditional model	**Fixed effect**	**β/Estimate (SE)**	***t***	***p*-value**	**-2LL**	**ICC**	
	Intercept	5.116 (0.149)	34.285	*p*<0.001	3083.268	0.439	*p*<0.01
	Variance	**β/Estimate (SE)**	***z***	***p*-value**			
	Residual	1.726 (0.087)	19.943	*p*<0.001			
	Intercept	1.351 (0.265)	5.103	*p*<0.001			
2. Unconditional linear growth model	**Fixed effect**	**β/Estimate (SE)**	***t***	***p*-value**	**-2LL**	**ICC**	**χ^2 diff, (Model 2-1) *p*-value**
	Intercept	4.648 (0.159)	29.224	*p*<0.001	3038.194	0.444	45.074, *p*<0.01
	Time	0.057 (0.008)	7.387	*p*<0.001			
	Variance	**β/Estimate (SE)**	***z***	***p*-value**			
	Residual	1.623 (0.081)	19.939	*p*<0.001			
	Intercept	1.295 (0.252(	5.142	*p*<0.001			
3. Unconditional linear growth model (allowing slope variation)	**Fixed effect**	**β/Estimate (SE)**	***t***	***p*-value**	**-2LL**	**ICC**	**χ^2 diff, (Model 3-2) *p*-value**
	Intercept	4.667 (0.147)	31.698	*p*<0.001	3013.159	0.412	25.035, *p*<0.01
	Time	0.054 (0.011)	4.792	*p*<0.001			
	Variance	**β/Estimate (SE)**	***z***	***p*-value**			
	Residual	1.511 (0.078)	19.266	*p*<0.001			
	Intercept (+ TIME)	1.060 (0.264)	4.009	*p*<0.001			
4. Add within-subjects variance autoregressive structure	**Fixed effect**	**β/Estimate (SE)**	***t***	***p*-value**	**-2LL**	**ICC**	**χ^2 diff, (Model 4-3) *p*-value**
	Intercept	4.665 (0.147)	31.751	*p*<0.001	3000.946	0.371	12.213, *p*<0.01
	Time	0.054 (0.011)	4.846	*p*<0.001			
	Variance	**β/Estimate (SE)**	***z***	***p*-value**			
	AR1 diagonal Residual	1.576 (0.090)	17.551	*p*<0.001			
	Intercept (+ TIME)	0.928 (0.269)	3.478	p=0.001			
5a. Adding PPRF to explain growth	**Fixed effect**	**β/Estimate (SE)**	***t***	***p*-value**	**-2LL**	**ICC**	**χ^2 diff, (Model 5a-4) *p*-value**
	Intercept	4.797 (0.373)	12.849	*p*<0.001	1400.99	0.546	1599.956, *p*<0.01
	Time	0.025 (0.036)	0.707	*p*=0.480			
	PPRF	0.005 (0.006)	0.925	*p*=0.356			
	PPRF*TIME	0.000 (0.000)	0.510	*p*=0.611			
	Variance	**β/Estimate (SE)**	***z***	***p*-value**			
	AR1 diagonal Residual	1.31 (0.117)	11.195	*p*<0.001			
	Intercept (+ TIME)	1.576 (0.566)	1.329	*p*=0.184			

Table 7. continued

5b. Adding PQSA to explain growth	**Fixed effect**	**β/Estimate (SE)**	***t***	***p*-value**	**-2LL**	**ICC**	**χ^2 diff, (Model 5b-4) *p*-value**
	Intercept	4.394 (0.294)	14.955	*p*<0.001	777.903	0.490	2223.043, *p*<0.01
	Time	-0.042 (0.033)	-1.265	*p*=0.210			
	PQSA	0.104 (0.054)	1.955	*p*=0.053			
	PQSA*TIME	0.012 (0.005)	2.345	*p*=0.022			
	Variance	**β/Estimate (SE)**	***z***	***p*-value**			
	AR1 diagonal Residual	1.254 (0.180)	6.958	*p*<0.001			
	Intercept (+ TIME)	1.204 (0.417)	2.889	p=0.004			
5c. Adding PQIDE to explain growth	**Fixed effect**	**β/Estimate (SE)**	***t***	***p*-value**	**-2LL**	**ICC**	**χ^2 diff, (Model 5c-4) *p*-value**
	Intercept	4.347 (0.321)	13.546	*p*<0.001	749.209	0.565	2251.737, *p*<0.01
	Time	-0.002 (0.382)	-0.052	*p*=0.959			
	PQIDE	0.071 (0.049)	1.438	*p*=0.153			
	PQIDE*TIME	0.007 (0.005)	1.307	*p*=0.194			
	Variance	**β/Estimate (SE)**	***z***	***p*-value**			
	AR1 diagonal Residual	1.073 (0.184)	5.848	*p*<0.001			
	Intercept (+ TIME)	1.394 (0.536)	2.601	*p*=0.009			

2.5 Discussion

2.5.1 Main findings

This study set out to investigate the effectiveness and change processes in a CBASP group run in a community setting, by modelling the change in skill acquisition and symptoms over the course of a 20-week group.

2.5.1.1 Effectiveness of CBASP-G intervention

The paired t-tests confirm that the CBASP-G intervention leads to a significant reduction in depression symptoms (BDI-II) with a large effect size, a significant decrease in overall distress (CORE-10) with a medium effect size and a significant medium to large effect size of improvement in self-reported mood score. The multilevel modelling indicated that the change in Mood and CORE-10 score was linear and not quadratic, aligning with Bird, (2016) and suggesting that symptom change happens steadily during CBASP-G. The unconditional models highlighted a substantial variance between participants for CORE-10 and Mood scores and that the starting score was not indicative of the subsequent rate of change. Adding time into the model significantly improved the fit indicating that Mood and distress (CORE-10) significantly improved during the group. Adjusting the model to allow slope variation by adding time into the random effects showed that patients experience change differently. They start at differing levels of distress and Mood scores and improve at different rates, while the initial Mood or CORE-10 score did not affect the pattern of change. The addition of the auto-regressive structure again improved the model fit significantly and as expected highlighted the correlation of adjacent time points in the scores and helping to explain more of the variance.

The global functioning scores (PGI, CGI-I and CGI-S) indicated there was significant overall improvement while the majority of participants (88.2%) had reductions in their self-rated severity of symptoms with the rest having no change. The clinician rating (PGI) indicated significantly that 70.5% improved with the others having no change.

2.5.1.1.1 Interpersonal functioning

Not enough data was present to add the interpersonal measures to the model. The change in overall interpersonal functioning as measured by the IIP-32 was not significant, however, there was significant change in the domain Hostile-submissive and this linked to decrease in depression scores which fits with previous research (Bird et al., 2018, Constantino et al., 2008; Constantino et al., 2012). It is possible that the missing data left this measure under powered and since change is likely to continue post group (Arnow et al., 2000, Arnow & Constantino, 2003), it may improve over time after the group ends.

2.5.1.2 Acquisitional learning and symptom change

Adding the measures of learning acquisition to the model improved the fit and helped explain significantly more of the variance between participants. The addition of PPRF and PQ-IDE did not have a significant fixed effect however, possibly due to a low sample size and not enough power, or perhaps due to this part of learning taking longer to deliver symptom change. Discriminating others more generally from the SO is likely to be a process of building trust with the therapist, the group and then testing this more generally which might take longer than the change in behaviour with the PQ-SA. Since, this measure was changed at Group 8 to include others more generally the results of this are inconclusive. The PQ-SA did have a significant impact on both the CORE-10 and Mood models and explained more of the variance making Time non-significant. For the CORE-10 model the PQ-SA achievement was stable over time but for Mood the association of PQ-SA was over time. This suggests that

the measure of learning acquisition is more important to change in CORE-10 score than the other elements added; time becomes less important due to the large variance caused by the additions of PQ-SA and IDE. A larger sample with more power and longer follow up might show significance for Time too. This fits with the evidence that achievement of core skill of CBASP has an effect on improving symptoms (Klein et al., 2011; Santiago et al., 2005).

McCullough's (2020) graph of skill acquisition and depression change (Figure 7.) does not represent the findings in this study. Change in symptoms (CORE-10 and Mood) was found to be linear not quadratic as depicted by McCullough (2020). However, the linear change in symptoms did fit with previous research by Bird (2016). This indicates that the change in symptoms is steadier through therapy. The skill acquisition change was quadratic in nature, and this points to the learning being quite steep at the start to middle of therapy and then levelling off, as might be expected as there is a ceiling to the measures of learning a skill. As the person implements their learning in daily life, gradually over time, this leads to symptom change. This shows us that while skills acquisition levels off towards end of therapy the symptoms keep changing steadily.

2.5.1.3 Group effect

Adding the fixed effect of Group into the model had mixed results. An initial effect of Group over time appeared significant for one group (Group 9) and on further investigation it was discovered that all but one participant dropped out of that group by midpoint of therapy, so the last participant had in effect 1-1 CBASP rather than group CBASP for the last half of therapy. This is likely to have skewed the effect of group, and on removing Group 9 there was no significant group effect. This may highlight that group membership has some effect on outcome, and indeed there will be different drop-out rates for each group.

2.5.2 Theoretical implications

These findings broadly fit with the evidence base that CBASP is effective for reducing depression and distress and increasing mood of participants (Furukawa et al., 2018; Keller et al., 2000; Kriston et al., 2014; Negt et al., 2016; Schramm et al., 2011; Wiersma et al., 2014) and that this group format of CBASP in an outpatient setting is effective (Locke et al., 2016; Michalak et al., 2015; Sayegh et al., 2012; Sabaβ et al., 2017).

The change in the interpersonal domains of hostile, submissive and hostile submissive support the findings of previous research that interpersonal change happens as a result of CBASP treatment and that these are the key areas of relevance to PDD (Bird et al., 2018; Constantino et al., 2008; Constantino et al., 2012; Köhler et al., 2019). However, only the hostile-submissive domain reached significance and it is possible that the sample was not big enough to detect changes in hostility or submissiveness independently. The effect size of change in hostile-submissive rating was slightly higher than Guhn et al.'s (2021b) study of group CBASP in an inpatient setting (in this study *d*=0.673 versus *d*=0.625 in Guhn et al., 2021b). This is interesting since the dose of therapy was higher in the inpatient study (24 individual and 24 group sessions over 12 weeks) and might indicate the inpatient sample needed a higher number of sessions to match the interpersonal change seen in this sample, possibly due to higher severity of symptoms. The finding that hostile-submissive traits were reduced by CBASP-G adds weight to the theory that becoming competent at the SA, and being more skilled interpersonally, helped improve symptoms (Klein et al., 2011; Santiago et al., 2005). It is possible that positive changes in the therapeutic relationship facilitated this with the reduction of the hostile-submissive interpersonal type (Klein et al., 2020).

The effect of the group attended was inconclusive, and this highlights the importance of the selection of participants suitable for groups. COVID-19 had an impact on the last group with it being held mostly over the phone and online. This could be a factor in the last group experiencing more distress due to the pandemic or give fewer opportunities to experience the impact of group effects and practice interpersonal learning in social situations. Little is known about the differences that the group element might have brought, and further studies could investigate patient experiences qualitatively (Guhn et al., 2021b).

The multilevel modelling indicated that skill acquisition explained a large part of the variance, but larger samples and/or a longer follow up may be needed to give greater clarity to this result and to review if other interpersonal domains reduce, and PQ-IDE and PPRF reach significance. The dropout rate for this study was substantial and this fits with the evidence that people with PDD are more likely to discontinue treatment for various reasons, such as inferior social support or higher side effects of medication linked to CM (Keller et al., 2014; Medeiros et al., 2021). The issues with many different confounding factors and moderators persists and any conclusions are tentative (Jobst et al., 2015; Kraemer, 2013). The findings are limited as the impact of the intervention cannot be separated from aspects such as the group setting, peer interaction, co-morbid mental health conditions, early onset depression, CM, social support and many more factors.

2.5.3 Strengths and Limitations

This study has some strengths; this is a “real life” clinical example of bringing theory from RCT evidence into practical therapy for people with PDD in the community. There was data from a substantial number of participants (80) and the use of multilevel modelling helped maximise the information gained. This is an example of clinical trials put into real life therapy situation with participants not excluded from treatment due to co-morbidities or health conditions (Angst

et al., 2008; Murphy & Byrne, 2012; Pettit et al., 2008; Trivedi et al., 2006). Assessments in outpatient settings do not have exclusion criteria comparable with clinical trials; suicidality, co-morbid physical and mental health conditions are the norm especially for those with PDD (Schramm et al. 2017). The skill and diligence of the therapists to engage and maintain this intensive therapy using DPI is an important strength of this study. DPI is likely to help people with several co-morbidities to engage in treatment, which is important with PDD being a difficult to treat presentation (McCullough, 2006).

Limitations of this study include that the outcome measures are mainly self-report, subjective and there may be a bias in the patient wanting to please the therapist, or the therapist rated scores being inflated. The PPRF filled in by the therapists to assess how well the patient has completed their SA not what their actual functioning is. It is possible that a person could be competent at filling these in and score well in session, but still be functioning poorly in real-life. Though, the remediation of the SA in session helps the patient understand how they might achieve their desired outcome next time so demonstrating that learning leads to symptom change. A limitation of the SA is that it is dependent on the person's choice of interpersonal difficulty; the subjective choice of an "easy" or "hard" one means there will be variance in the scores (Santiago et al., 2005). Moreover, this study measured distress (CORE-10) and Mood and therefore, did not mirror McCullough's (2020) theorised change in depression symptoms. There is a considerable amount of missing data in this sample, due to the "real-world" circumstance of this study and that people might drop-out due to feeling better, or feeling worse, or feeling apathetic about the group. Although the data was deemed to be missing at random, it would be helpful to know reasons for dropout to be able to assess this in more detail. A more robust examination on the patterns of missing data and the likely effect of this would give greater understanding of the validity of the research findings. Additionally, the lack of follow up data means that any improvement gained after the group as expected is not captured (Schramm et al., 2019). The length

of intervention at 20 weeks is lower compared to Schramm et al. (2017) with a total contact time of 48 weeks and drop-out rates appear to be high. This is an important point since interpersonal change is expected to continue to deliver improvements in symptoms after the 20 weeks of therapy finishes. The linear change in symptoms could have a different curve fit over a longer follow up period and this means the measures should be collected for substantially longer to understand the full impact of learning on reducing distress and improving mood.

Due to the post-hoc nature of this study, there was little demographic information available and there are many variables that cannot be accounted for. It is possible that some participants were on varying anti-depressant medication and had a bigger burden of side effect or that some of the side effects are mirrored in depression outcome BDI-II (Hieronymus et al., 2021; Medeiros et al., 2021). It is not known what percentage of participants had a CM history since there was no measure of CM taken, and information was not collected on early-onset depression, (Klein et al., 2015; Nelson et al., 2017) or if participants had less severe symptoms and higher quality of life; therefore, it is possible that some of these individuals would have benefited from a different type of therapy such as supportive therapy as in Schramm et al. (2017). Conversely, the opposite could be true, that the sample had more CM and that this stopped them from making progress in CBASP (Bausch et al., 2017; Nanni et al., 2012). Baseline interpersonal style might also affect the efficacy of the group. If a higher proportion of hostile-dominant types in the sample some may have benefited from a different type of therapy, and this was not examined (Probst et al., 2020). Indeed, there were several challenges presented working with a secondary dataset (rather than planned research) that were unavoidable due to COVID-19 but would have impacted on the robustness of this research. These include the control and consistency of the measures selected, having follow up data, the ability to source missing data with expedience, greater access to demographic and clinical information and the ability to examine

broader research questions. These factors would have added a depth to the analysis and given the research greater focus and very possibly clearer results which could inform current knowledge and future research directions in a more potent way and the secondary nature of the dataset should be considered a major limitation for this study.

2.5.4 Future research

There are many areas of interest to be pursued following this study. An analysis of dropouts and missing data could investigate the reasons involved. Issues such as the impact of anti-depressant use, CM, early versus late onset of depression, baseline quality of life and interpersonal type scores are important variables that have not been considered here but are likely to have had some impact. Further studies should examine any group effects in detail and the long-term efficacy and efficacy of maintenance groups. (Arnow & Constantino, 2003). This would help focus the CBASP-G delivery to those that are most likely to benefit and fits with the suggestion that individual tailoring of treatment could bring better results (Furukawa et al. 2018). Patient preference for type of therapy could be considered to improve efficacy and drop-out rates (Mergl et al., 2011; Swift et al., 2011; Williams et al., 2016). Additional studies could look at using a short measure like the PHQ-9 to assess depression symptoms to model change and using an independent rater would add weight to measures such as the PPRF and depression measures, though it is acknowledged that this would be hard to implement in every-day practice.

In summary, CBASP-G was found to be an effective intervention for improving mood and overall distress for individuals presenting with persistent depression in a community setting. Skill acquisition was found to be an important factor in the reduction of symptoms across therapy. It is vitally important that interventions are finely tuned using robust evidence so persistently depressed people in our communities get the support they need. Furthermore, this

assistance should be of the correct dose and maintenance support offered as the literature recommends (Jobst et al., 2015; Pettit et al., 2008; Rubio et al., 2011).

2.6 References

Angst, J., Gamma, A., Rössler, W., Ajdacic, V. & Klein, D. N. (2008). Long-term depression versus episodic major depression: Results from the prospective Zurich study of a community sample. *Journal of affective disorders, 115*(1), 112-121. doi:10.1016/j.jad.2008.09.023

Arnow, B. A. & Constantino, M. J. (2003). Effectiveness of psychotherapy and combination treatment for chronic depression. *Journal of clinical psychology, 59*(8), 893-905. doi:10.1002/jclp.10181

Barkham, M., Bewick, B., Mullin, T., Gilbody, S., Connell, J., Cahill, J., et al. (2013). The CORE-10: A short measure of psychological distress for routine use in the psychological therapies. *Counselling and psychotherapy research, 13*(1), 3-13. doi:10.1080/14733145.2012.729069

Barnhofer, T., Crane, C., Hargus, E., Amarasinghe, M., Winder, R. & Williams, J. M. G. (2009). Mindfulness-based cognitive therapy as a treatment for chronic depression: A preliminary study. *Behaviour Research and Therapy, 47*(5), 366-373. doi:http://dx.doi.org/10.1016/j.brat.2009.01.019

Bausch, P., Fangmeier, T., Zobel, I., Schoepf, D., Drost, S., Schnell, K., et al. (2017). The impact of childhood maltreatment on the differential efficacy of CBASP versus escitalopram in patients with chronic depression: A secondary analysis. *Clinical psychology & psychotherapy, 24*(5), 1155-1162. doi:http://dx.doi.org/10.1002/cpp.2081

Beck, A. T., Steer, R. A., Ball, R. & Ranieri, W. F. (1996). Comparison of Beck Depression Inventories-IA and-II in Psychiatric Outpatients. *Journal of personality assessment, 67*(3), 588-597. doi:10.1207/s15327752jpa6703_13

Beck AT, Steer RA, Brown GK. *BDI-II: Beck Depression Inventory Manual*. 2nd edn. San Antonio,TX: Psychological Corporation, 1996.

Bird, T. (2016). *Do chronically depressed individuals exhibit a hostile-submissive interpersonal style and what is the process of change in Cognitive Behavioural Analysis system of psychotherapy?* , The University of Edinburgh.

Bird, T., Tarsia, M. & Schwannauer, M. (2018). Interpersonal styles in major and chronic depression:A systematic review and meta-analysis. *Journal of Affective Disorders*. 239, p. 93-101.

Blalock, J. A., Fouladi, R. T., Cinciripini, P. M., Markowitz, J. C., Klein, D. N., Rothbaum, B. O., et al. (2008). Cognitive and Behavioral Mediators of Combined Pharmacotherapy and Psychotherapy of Chronic Depression. *Cognitive therapy and research, 32*(2), 197-211. doi:10.1007/s10608-006-9092-z

Caspi, A., Houts, R. M., Ambler, A., Danese, A., Elliott, M. L., Hariri, A., et al. (2020). Longitudinal Assessment of Mental Health Disorders and Comorbidities Across 4 Decades Among Participants in the Dunedin Birth Cohort Study. *JAMA network open, 3*(4), e203221-e203221. doi:10.1001/jamanetworkopen.2020.3221

Cicchetti, D., & Barnett, D. (1991). Attachment organization in maltreated preschoolers. *Development and Psychopathology*, 3, 397–411.

Constantino, M. J., Laws, H. B., Arnow, B. A., Klein, D. N., Rothbaum, B. O. & Manber, R. (2012). The relation between changes in patients' interpersonal impact messages and outcome in treatment for chronic depression. *Journal of Consulting and Clinical Psychology, 80*(3), 354-364. doi:http://dx.doi.org/10.1037/a0028351

Constantino, M. J., Manber, R., DeGeorge, J., McBride, C., Ravitz, P., Zuroff, D. C., et al. (2008). INTERPERSONAL STYLES OF CHRONICALLY DEPRESSED OUTPATIENTS: PROFILES AND THERAPEUTIC CHANGE. *Psychotherapy, 45*(4), 491-506. doi:http://dx.doi.org/10.1037/a0014335

Cuijpers, P., Noma, H., Karyotaki, E., Cipriani, A. & Furukawa, T. A. (2019). Effectiveness and Acceptability of Cognitive Behavior Therapy Delivery Formats in Adults With Depression: A Network Meta-analysis. *JAMA psychiatry (Chicago, Ill.), 76*(7), 700-707. doi:10.1001/jamapsychiatry.2019.0268

Cukrowicz, K. C. & Joiner Jr, T. E. (2007). Computer-Based Intervention for Anxious and Depressive Symptoms in a Non-Clinical Population. *Cognitive therapy and research, 31*(5), 677-693. doi:10.1007/s10608-006-9094-x

Diagnostic and statistical manual of mental disorders : DSM-5. (2013). (Fifth edition. ed.). Arlington, VA: American Psychiatric Association.

Domes, G., Normann, C. & Heinrichs, M. (2016). The effect of oxytocin on attention to angry and happy faces in chronic depression. *BMC Psychiatry, 16*(1), 92. doi:http://dx.doi.org/10.1186/s12888-016-0794-9

Field, A. (2013). *Discovering statistics using IBM SPSS statistics* (4th ed.). SAGE Publications.

Furukawa, T. A., Efthimiou, O., Weitz, E. S., Cipriani, A., Keller, M. B., Kocsis, J. H., et al. (2018). Cognitive-behavioral analysis system of psychotherapy, drug, or their combination for persistent depressive disorder: Personalizing the treatment choice using individual participant data network metaregression. *Psychotherapy and Psychosomatics, 87*(3), 140-153. doi:http://dx.doi.org/10.1159/000489227

Gilmer, W. S., Trivedi, M. H., Rush, A. J., Wisniewski, S. R., Luther, J., Howland, R. H., et al. (2005). Factors associated with chronic depressive episodes: a preliminary report from the STAR-D project. *Acta psychiatrica Scandinavica, 112*(6), 425-433. doi:10.1111/j.1600-0447.2005.00633.x

Guhn, A., Köhler, S., Brakemeier, E.-L. & Sterzer, P. (2021a). Cognitive Behavioral Analysis System of Psychotherapy for inpatients with persistent depressive disorder: a naturalistic trial on a general acute psychiatric unit.

European archives of psychiatry and clinical neuroscience, 271(3), 495-505. doi:10.1007/s00406-019-01038-5

Guhn, A., Schön, D., Zische, Y., Sterzer, P. & Köhler, S. (2021b). Interpersonal Change During Inpatient CBASP Treatment: Focus on Group Therapy. *Frontiers in psychiatry, 12*, 620037-620037. doi:10.3389/fpsyt.2021.620037

Guhn, A., Sterzer, P., Haack, F. H. & Köhler, S. (2018). Affective and cognitive reactivity to mood induction in chronic depression. *Journal of affective disorders, 229*, 275-281. doi:10.1016/j.jad.2017.12.090

Guy W (ed). (1976). ECDEU Assessment Manual for Psychopharmacology. Rockville, MD: US Department of Heath,Education, and Welfare Public Health Service Alcohol, Drug Abuse, and Mental Health Administration, 1976 (Full text manual)

Guy, W. (2000). "Clinical Global Impressions (CGI) Scale, Modified". In Rush, John A.; Task Force for the Handbook of Psychiatric Measures (eds.). *Handbook of Psychiatric Measures*(1st ed.). Washington, DC: American Psychiatric Association.

Hewlett, E. and V. Moran (2014), *Making Mental Health Count: The Social and Economic Costs of Neglecting Mental Health Care*, OECD Health Policy Studies, OECD Publishing, Paris, https://doi.org/10.1787/9789264208445-en.

Hieronymus, F., Lisinski, A., Eriksson, E. & Østergaard, S. D. (2021). Do side effects of antidepressants impact efficacy estimates based on the Hamilton Depression Rating Scale? A pooled patient-level analysis. *Translational psychiatry, 11*(1), 249-249. doi:10.1038/s41398-021-01364-0

Horowitz, L. M., Alden, L. E., Wiggins, J. S., et al (2000). *IIP - Inventory of Interpersonal Problems Manual*. San Antonio, TX: The Psychological Corporation.

IBM Corp. Released (2017). IBM SPSS Statistics for Macintosh, Version 25.0. Armonk, NY: IBM Corp.

Ijaz, S., Davies, P., Williams, C. J., Kessler, D., Lewis, G. & Wiles, N. (2018). Psychological therapies for treatment-resistant depression in adults. *Cochrane Database of Systematic Reviews, 2018*(5), CD010558. doi:http://dx.doi.org/10.1002/14651858.CD010558.pub2

Jakobsen, J. C., Gluud, C., Wetterslev, J. & Winkel, P. (2017). When and how should multiple imputation be used for handling missing data in randomised clinical trials - a practical guide with flowcharts. *BMC medical research methodology, 17*(1), 162-162. doi:10.1186/s12874-017-0442-1

Jobst, A., Brakemeier, E. L., Buchheim, A., Caspar, F., Cuijpers, P., Ebmeier, K. P., et al. (2015). European Psychiatric Association Guidance on psychotherapy in chronic depression across Europe. *European psychiatry, 33*(1), 18-36. doi:10.1016/j.eurpsy.2015.12.003

Keller, M. B., McCullough, J. P., Klein, D. N., Arnow, B., Dunner, D. L., Gelenberg, A. J., et al. (2000). A comparison of nefazodone, the cognitive behavioral-analysis system of psychotherapy, and their combination for the treatment of chronic depression. *New England Journal of Medicine, 342*(20), 1462-1470. doi:http://dx.doi.org/10.1056/NEJM200005183422001

Keller, S. M., Feeny, N. C. & Zoellner, L. A. (2014). Depression Sudden Gains and Transient Depression Spikes During Treatment for PTSD. *Journal of consulting and clinical psychology, 82*(1), 102-111. doi:10.1037/a0035286

Kendrick, T. (2021). Strategies to reduce use of antidepressants. *British journal of clinical pharmacology, 87*(1), 23-33. doi:10.1111/bcp.14475

Klein, D. N., Arnow, B. A., Barkin, J. L., Dowling, F., Kocsis, J. H., Leon, A. C., et al. (2009). Early adversity in chronic depression: clinical correlates and response to pharmacotherapy. *Depression and Anxiety, 26*(8), 701-710. doi:10.1002/da.20577

Klein, D. N., Leon, A. C., Li, C., D'Zurilla, T. J., Black, S. R., Vivian, D., et al. (2011). Social problem solving and depressive symptoms over time: A randomized clinical trial of cognitive-behavioral analysis system of psychotherapy, brief supportive psychotherapy, and pharmacotherapy. *Journal of Consulting and Clinical Psychology, 79*(3), 342-352. doi:http://dx.doi.org/10.1037/a0023208

Klein, D. N., Schwartz, J. E., Santiago, N. J., Vivian, D., Vocisano, C., Castonguay, L. G., et al. (2003). Therapeutic Alliance in Depression Treatment: Controlling for Prior Change and Patient Characteristics. *Journal of consulting and clinical psychology, 71*(6), 997-1006. doi:10.1037/0022-006X.71.6.997

Klein, Jan P., Probst, T., Kriston, L., Assmann, N., Bailer, J., Eich, H., et al. (2020). Changes in Therapeutic Alliance and in Social Inhibition as Mediators of the Effect of the Cognitive Behavioral Analysis System of Psychotherapy: A Secondary Analysis from a Randomized Clinical Trial. *Psychotherapy and psychosomatics, 89*(4), 261-262. doi:10.1159/000506082

Klein, J. P., Roniger, A., Schweiger, U., Spath, C. & Brodbeck, J. (2015). The association of childhood trauma and personality disorders with chronic depression: A cross-sectional study in depressed outpatients. *Journal of Clinical Psychiatry 76(6):e794-801, 2015 Jun, 76*(6), e794-801.

Kraemer, H. C. (2013). Discovering, comparing, and combining moderators of treatment on outcome after randomized clinical trials: a parametric approach. *Statistics in medicine, 32*(11), 1964-1973. doi:10.1002/sim.5734

Kriston, L., von Wolff, A., Westphal, A., Holzel, L. P. & Harter, M. (2014). Efficacy and acceptability of acute treatments for persistent depressive disorder: A network meta-analysis. *Depression and Anxiety, 31*(8), 621-630.

Krystal, J. H., Rosenheck, R. A., Cramer, J. A., Vessicchio, J. C., Jones, K. M., Vertrees, J. E., et al. (2011). Adjunctive Risperidone Treatment for Antidepressant-Resistant Symptoms of Chronic Military Service–Related PTSD: A Randomized Trial. *JAMA : the journal of the American Medical Association, 306*(5), 493-502. doi:10.1001/jama.2011.1080

Köhler, S., Chrysanthou, S., Guhn, A. & Sterzer, P. (2019). Differences between chronic and nonchronic depression: Systematic review and implications for treatment. *Depression and anxiety, 36*(1), 18-30. doi:10.1002/da.22835

Laerd Statistics. 2015. *One-way ANOVA with repeated measures in SPSS Statistics - Understanding and reporting the output.*. [online] Available at: <https://statistics.laerd.com/spss-tutorials/one-way-anova-repeated-measures-using-spss-statistics-2.php> [Accessed 17 February 2015].

Leader, J. B. & Klein, D. N. (1996). Social adjustment in dysthymia, double depression and episodic major depression. *Journal of affective disorders, 37*(2), 91-101. doi:10.1016/0165-0327(95)00076-3

Lewinsohn, P. M. & Clarke, G. N. (1999). Psychosocial treatments for adolescent depression. *Clinical psychology review, 19*(3), 329-342. doi:10.1016/S0272-7358(98)00055-5

Locke, K. D., Sayegh, L., Penberthy, J. K., Weber, C., Haentjens, K. & Turecki, G. (2017). Interpersonal Circumplex Profiles Of Persistent Depression: Goals, Self-Efficacy, Problems, And Effects Of Group Therapy. *Journal of clinical psychology, 73*(6), 595-611. doi:10.1002/jclp.22343

Manber, R., Arnow, B., Blasey, C., Vivian, D., McCullough, J. P., Blalock, J. A., et al. (2003). Patient's therapeutic skill acquisition and response to

psychotherapy, alone or in combination with medication. *Psychological Medicine, 33*(4), 693-702. doi:http://dx.doi.org/10.1017/S0033291703007608

McCullough, J. J. P. (2020). Characteristics of the Optimal Cognitive Behavioral Analysis System of Psychotherapy (CBASP) Therapist Role. *Frontiers in psychiatry, 11*, 609954-609954. doi:10.3389/fpsyt.2020.609954

McCullough, J. P. (2000). *Treatment for chronic depression : cognitive behavioral analysis system of psychotherapy (CBASP) / James P. McCullough, Jr. ; foreword by Marvin R. Goldfied*. New York: Guilford Press.

McCullough Jr, J. P. (2003). Treatment for chronic depression using Cognitive Behavioral Analysis System of Psychotherapy (CBASP). *Journal of Clinical Psychology, 59*(4), 833-846. doi:10.1002/jclp.10176

McCullough J.P. (2006). Treating Chronic Depression with Disciplined Personal Involvement: Cognitive Behavioral Analysis System of Psychotherapy (CBASP). Richmond: Springer.

McHugh, R. K., Whitton, S. W., Peckham, A. D., Welge, J. A. & Otto, M. W. (2013). Patient preference for psychological vs pharmacologic treatment of psychiatric disorders: A meta-analytic review. *The journal of clinical psychiatry, 74*(6), 595-602. doi:10.4088/JCP.12r07757

Medeiros, G. C., Prueitt, W. L., Rush, A. J., Minhajuddin, A., Czysz, A. H., Patel, S. S., et al. (2021). Impact of childhood maltreatment on outcomes of antidepressant medication in chronic and/or recurrent depression. *Journal of affective disorders, 291*, 39-45. doi:10.1016/j.jad.2021.04.022

Mergl, R., Henkel, V., Allgaier, A.-K., Kramer, D., Hautzinger, M., Kohnen, R., et al. (2011). Are Treatment Preferences Relevant in Response to Serotonergic Antidepressants and Cognitive-Behavioral Therapy in Depressed Primary Care Patients? Results from a Randomized Controlled Trial Including a Patients' Choice Arm. *Psychotherapy and psychosomatics, 80*(1), 39-47. doi:10.1159/000318772

Michalak, J., Schultze, M., Heidenreich, T. & Schramm, E. (2015). A randomized controlled trial on the efficacy of mindfulness-based cognitive therapy and a group version of cognitive behavioral analysis system of psychotherapy for chronically depressed patients. *Journal of Consulting and Clinical Psychology, 83*(5), 951-963. doi:http://dx.doi.org/10.1037/ccp0000042

Mohebbi, M., Dodd, S., Dean, O. M. & Berk, M. (2018). Patient centric measures for a patient centric era: Agreement and convergent between ratings on The Patient Global Impression of Improvement (PGI-I) scale and the Clinical Global Impressions – Improvement (CGI-S) scale in bipolar and major depressive disorder. *European psychiatry, 53*, 17-22. doi:10.1016/j.eurpsy.2018.05.006

Morrison, N. (2001). GROUP COGNITIVE THERAPY: TREATMENT OF CHOICE OR SUB-OPTIMAL OPTION? *Behavioural and cognitive psychotherapy, 29*(3), 311-332. doi:10.1017/S1352465801003058

Murphy, J. & Byrne, G. (2011). The failure to define: A systematic review of the conceptualisation of treatment resistant depression (TRD). *Australian and New Zealand Journal of Psychiatry, 45*(O1), A45.

Nanni, V., Uher, R. & Danese, A. (2012). Childhood Maltreatment Predicts Unfavorable Course of Illness and Treatment Outcome in Depression: A Meta-Analysis. *The American journal of psychiatry, 169*(2), 141-151. doi:10.1176/appi.ajp.2011.11020335

National Institute for Clinical Excellence, July 2017, draft for consultation. Depression in adults: treatment and management. Available at https://www.nice.org.uk/guidance/indevelopment/gid-cgwave0725

Negt, P., Brakemeier, E. L., Michalak, J., Winter, L., Bleich, S. & Kahl, K. G. (2016). The treatment of chronic depression with cognitive behavioral analysis system of psychotherapy: a systematic review and meta-analysis of

randomized-controlled clinical trials. *Brain and Behavior, 6*(8), e00486. doi:http://dx.doi.org/10.1002/brb3.486

Nelson, J., Klumparendt, A., Doebler, P. & Ehring, T. (2017). Childhood maltreatment and characteristics of adult depression: Meta-analysis. *British journal of psychiatry, 210*(2), 96-104. doi:10.1192/bjp.bp.115.180752

Nuebel, J., Guhn, A., Muellender, S., Le, H. D., Cohrdes, C. & Koehler, S. (2020). Persistent depressive disorder across the adult lifespan: results from clinical and population-based surveys in Germany. *BMC psychiatry, 20*(1), 58-58. doi:10.1186/s12888-020-2460-5

Paykel, E. S. (1987). Cognitive therapy and the emotional disorders: A. T. Beck. *British journal of psychiatry, 150*(6), 870-871. doi:10.1192/S0007125000214918

Pettit, J. W., Lewinsohn, P. M., Roberts, R. E., Seeley, J. R. & Monteith, L. (2008). The long-term course of depression: development of an empirical index and identification of early adult outcomes. *Psychological medicine, 39*(3), 403-412. doi:10.1017/S0033291708003851

Piaget. (1981). *Philosophical books, 22*(3), 143-143. doi:10.1111/j.1468-0149.1981.tb00999.x

Probst, T., Schramm, E., Heidenreich, T., Klein, J. P. & Michalak, J. (2020). Patients' interpersonal problems as moderators of depression outcomes in a randomized controlled trial comparing mindfulness-based cognitive therapy and a group version of the cognitive-behavioral analysis system of psychotherapy in chronic depression. *Journal of clinical psychology, 76*(7), 1241-1254. doi:http://dx.doi.org/10.1002/jclp.22931

Rhebergen, D. & Graham, R. (2014). The re-labelling of dysthymic disorder to persistent depressive disorder in DSM-5: old wine in new bottles? *Current opinion in psychiatry, 27*(1), 27-31. doi:10.1097/YCO.0000000000000022

Riihimaki, K. (2017). Health-related quality of life of primary care patients with depressive disorders. *European psychiatry, 41*(S1), S540-S540. doi:10.1016/j.eurpsy.2017.01.747

Riihimaki, K., Vuorilehto, M. & Isometsa, E. (2017). Maintenance pharmacotherapy for recurrent major depressive disorder in primary care: A 5-year follow-up study. *European Psychiatry, 41*, 111-114. doi:http://dx.doi.org/10.1016/j.eurpsy.2016.10.010

Rubio, J. M., Markowitz, J. C., Alegría, A., Pérez-Fuentes, G., Liu, S. M., Lin, K. H., et al. (2011). Epidemiology of chronic and nonchronic major depressive disorder: results from the national epidemiologic survey on alcohol and related conditions. *Depression and anxiety, 28*(8), 622-631. doi:10.1002/da.20864

Sabaß, L., Padberg, F., Normann, C., Engel, V., Konrad, C., Helmle, K., et al. (2018). Cognitive Behavioral Analysis System of Psychotherapy as group psychotherapy for chronically depressed inpatients: a naturalistic multicenter feasibility trial. *European archives of psychiatry and clinical neuroscience, 268*(8), 783-796. doi:10.1007/s00406-017-0843-5

Saha, K., Torous, J., Kiciman, E. & De Choudhury, M. (2021). Understanding Side Effects of Antidepressants: Large-scale Longitudinal Study on Social Media Data. *JMIR mental health, 8*(3), e26589-e26589. doi:10.2196/26589

Santiago, N. J., Klein, D. N., Vivian, D., Arnow, B. A., Blalock, J. A., Kocsis, J. H., et al. (2005). The Therapeutic Alliance and CBASP-Specific Skill Acquisition in the Treatment of Chronic Depression. *Cognitive therapy and research, 29*(6), 803-817. doi:10.1007/s10608-005-9638-5

Sayegh, L., Locke, K. D., Pistilli, D., Penberthy, J. K., Chachamovich, E., McCullough, J. P., et al. (2012). Cognitive Behavioural Analysis System of Psychotherapy for Treatment-Resistant Depression: Adaptation to a Group Modality. *Behaviour change, 29*(2), 97-108. doi:10.1017/bec.2012.2

Schindler, A. C., Hiller, W. & Witthoft, M. (2011). Benchmarking of cognitive-behavioral therapy for depression in efficacy and effectiveness studies--how do exclusion criteria affect treatment outcome? *Psychotherapy research : journal of the Society for Psychotherapy Research, 21*(6), 644-657.

Schramm, E., Kriston, L., Elsaesser, M., Fangmeier, T., Meister, R., Bausch, P., et al. (2019). Two-year follow-up after treatment with the cognitive behavioral analysis system of psychotherapy versus supportive psychotherapy for early-onset chronic depression. *Psychotherapy and Psychosomatics, 88*(3), 154-164. doi:http://dx.doi.org/10.1159/000500189

Schramm, E., Kriston, L., Zobel, I., Bailer, J., Wambach, K., Backenstrass, M., et al. (2017). Effect of disorder-specific vs nonspecific psychotherapy for chronic depression: A randomized clinical trial. *JAMA Psychiatry, 74*(3), 233-242. doi:http://dx.doi.org/10.1001/jamapsychiatry.2016.3880

Schramm, E., Zobel, I., Dykierek, P., Kech, S., Brakemeier, E. L., Kulz, A., et al. (2011). Cognitive behavioral analysis system of psychotherapy versus interpersonal psychotherapy for early-onset chronic depression: A randomized pilot study. *Journal of Affective Disorders, 129*(1-3), 109-116. doi:http://dx.doi.org/10.1016/j.jad.2010.08.003

Scottish Health Survey (2019) accessed on 08/06/021 https://www.gov.scot/publications/scottish-health-survey-2019-volume-1-main-report/pages/5/

Serbanescu, I., Walter, H., Schnell, K., Kessler, H., Weber, B., Drost, S., et al. (2020). Combining baseline characteristics to disentangle response differences to disorder-specific versus supportive psychotherapy in patients with persistent depressive disorder. *Behaviour Research and Therapy, 124*, 103512. doi:http://dx.doi.org/10.1016/j.brat.2019.103512

Swan, J. S., MacVicar, R., Christmas, D., Durham, R., Rauchhaus, P., McCullough, J. P., et al. (2013). Cognitive Behavioural Analysis System of

Psychotherapy (CBASP) for chronic depression: Clinical characteristics and six month clinical outcomes in an open case series. *Journal of affective disorders, 152*(1), 268-276. doi:10.1016/j.jad.2013.09.024

Swift, J. K. & Greenberg, R. P. (2012). Premature discontinuation in adult psychotherapy: A meta-analysis. *Journal of consulting and clinical psychology, 80*(4), 547-559. doi:10.1037/a0028226

Szpak, K. (2020). Does Cognitive Behavioural Analysis system of psychotherapy improve interpersonal functioning in patients affected by persistent depression and what can research tell us about the theoretical model this therapy is based on? : The University of Edinburgh.

The Matrix (2015). A Guide to Delivering Evidence-Based Psychological Therapies in Scotland. NHS Education Scotland (NES).

Torpey, D. C. & Klein, D. N. (2008). Chronic depression: Update on classification and treatment. *Current psychiatry reports, 10*(6), 458-464. doi:10.1007/s11920-008-0074-6

Trivedi, M. H., Rush, A. J., Wisniewski, S. R., Nierenberg, A. A., Warden, D., Ritz, L., et al. (2006). Evaluation of Outcomes With Citalopram for Depression Using Measurement-Based Care in STARD: Implications for Clinical Practice. *The American journal of psychiatry, 163*(1), 28-40. doi:10.1176/appi.ajp.163.1.28

Vivian, D. & Salwen, J. (2013). Key Process Issues in Cognitive Behavioral Analysis System of Psychotherapy (CBASP): Translation of an Evidence-Based Model Into Clinical Practice and Training. *Psychotherapy (Chicago, Ill.), 50*(3), 398-403. doi:10.1037/a0033054

Whitfield, G., 2010. Group cognitive–behavioural therapy for anxiety and depression. Advances in Psychiatric Treatment 16, 219–227.. doi:10.1192/apt.bp.108.005744

Wiersma, J. E., Hovens, J. G. F. M., van Oppen, P., Giltay, E. J., van Schaik, D. J. F., Beekman, A. T. F., et al. (2009). The Importance of Childhood Trauma and Childhood Life Events for Chronicity of Depression in Adults. *The journal of clinical psychiatry, 70*(7), 983-989. doi:10.4088/JCP.08m04521

Wiersma, J. E., Van Schaik, D. J., Hoogendorn, A. W., Dekker, J. J., Van, H. L., Schoevers, R. A., et al. (2014). The effectiveness of the cognitive behavioral analysis system of psychotherapy for chronic depression: A randomized controlled trial. *Psychotherapy and Psychosomatics, 83*(5), 263-269.

Wiersma, J. E., Van Schaik, D. J. F., Blom, M. B. J., Bakker, L., Van Oppen, P. & Beekman, A. T. F. (2009). Treatment for chronic depression: Cognitive behavioral analysis system of psychotherapy (CBASP). *Tijdschrift voor Psychiatrie, 51*(10), 727-736.

Williams, R., Farquharson, L., Palmer, L., Bassett, P., Clarke, J., Clark, D. M., et al. (2016). Patient preference in psychological treatment and associations with self-reported outcome: National cross-sectional survey in England and Wales. *BMC psychiatry, 16*(4), 4-4. doi:10.1186/s12888-015-0702-8

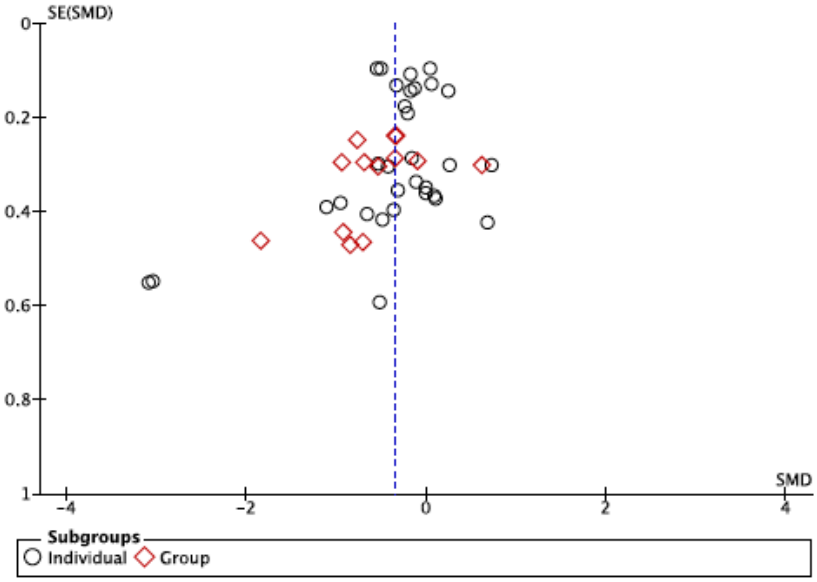
Wittchen, H. U., Jacobi, F., Rehm, J., Gustavsson, A., Svensson, M., Jönsson, B., et al. (2011). The size and burden of mental disorders and other disorders of the brain in Europe 2010. *European neuropsychopharmacology, 21*(9), 655-679. doi:10.1016/j.euroneuro.2011.07.018

World Health Organization. (2018). *International classification of diseases for mortality and morbidity statistics* (11th Revision). Retrieved from https://icd.who.int/browse11/l-m/en

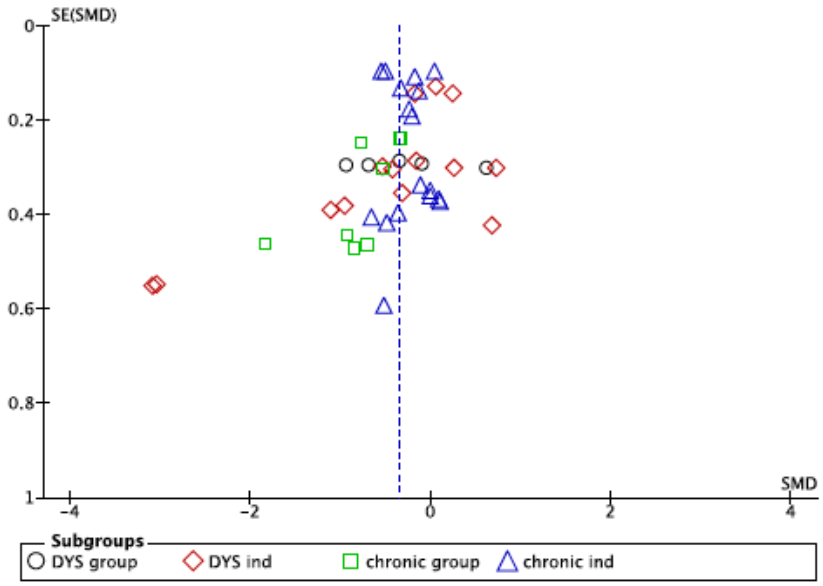
World Health Organization (2020). Depression Fact Sheet. Available from: http://www.who.int/en/news-room/fact-sheets/detail/depression

2.7 Appendices

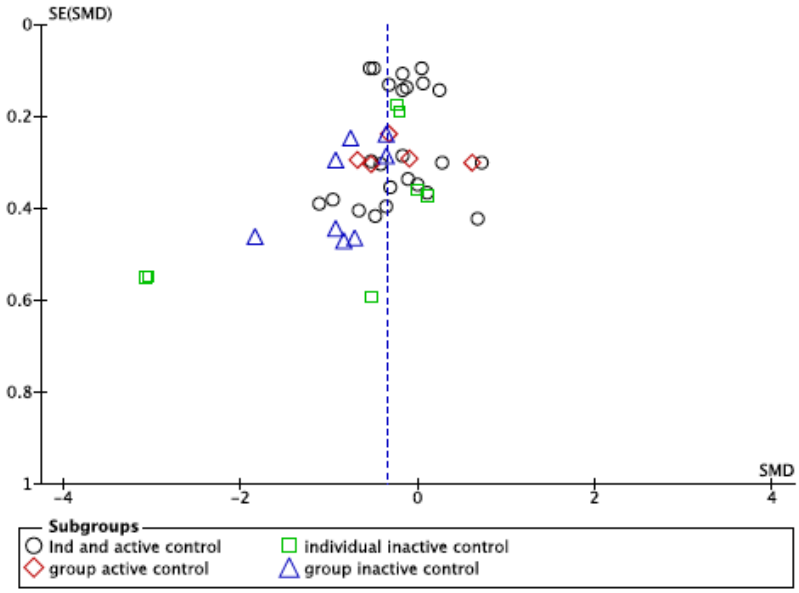
Appendix A. Funnel plots of meta-analysis



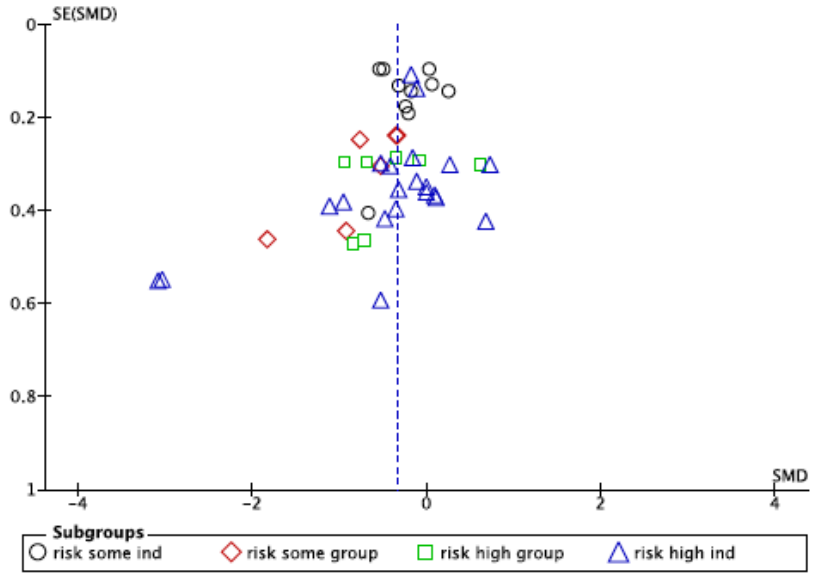
Funnel plot of Indvidual and groups



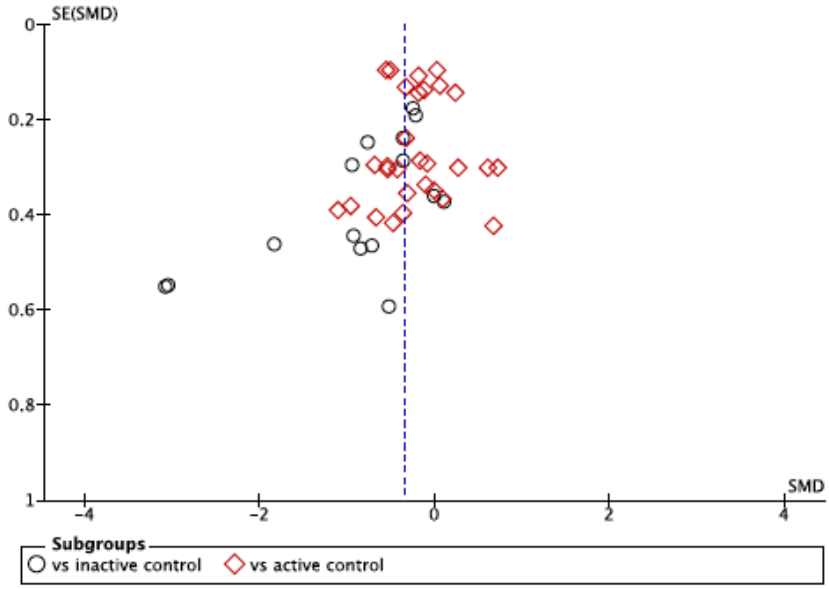
Funnel plot of Indvidual and groups by DYS and chronic depression



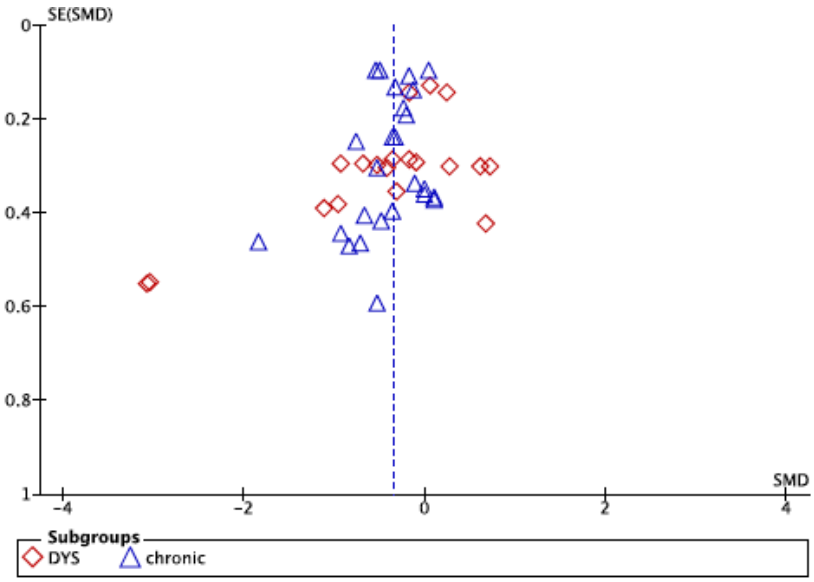
Funnel plot of Indvidual and groups and active inactive controls



Funnel plot of Indvidual and groups by risk



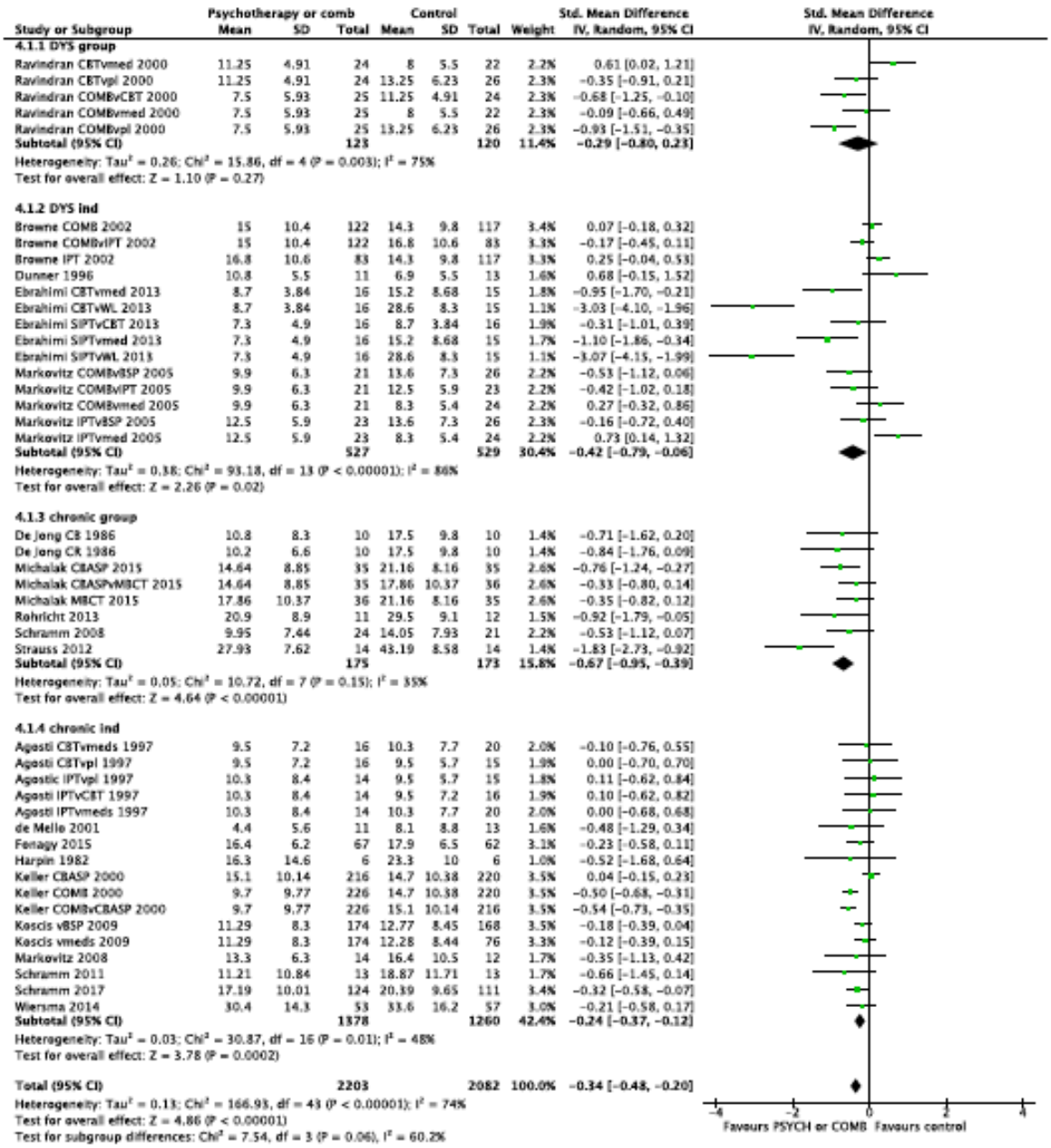
Funnel plot of inactive and active controls



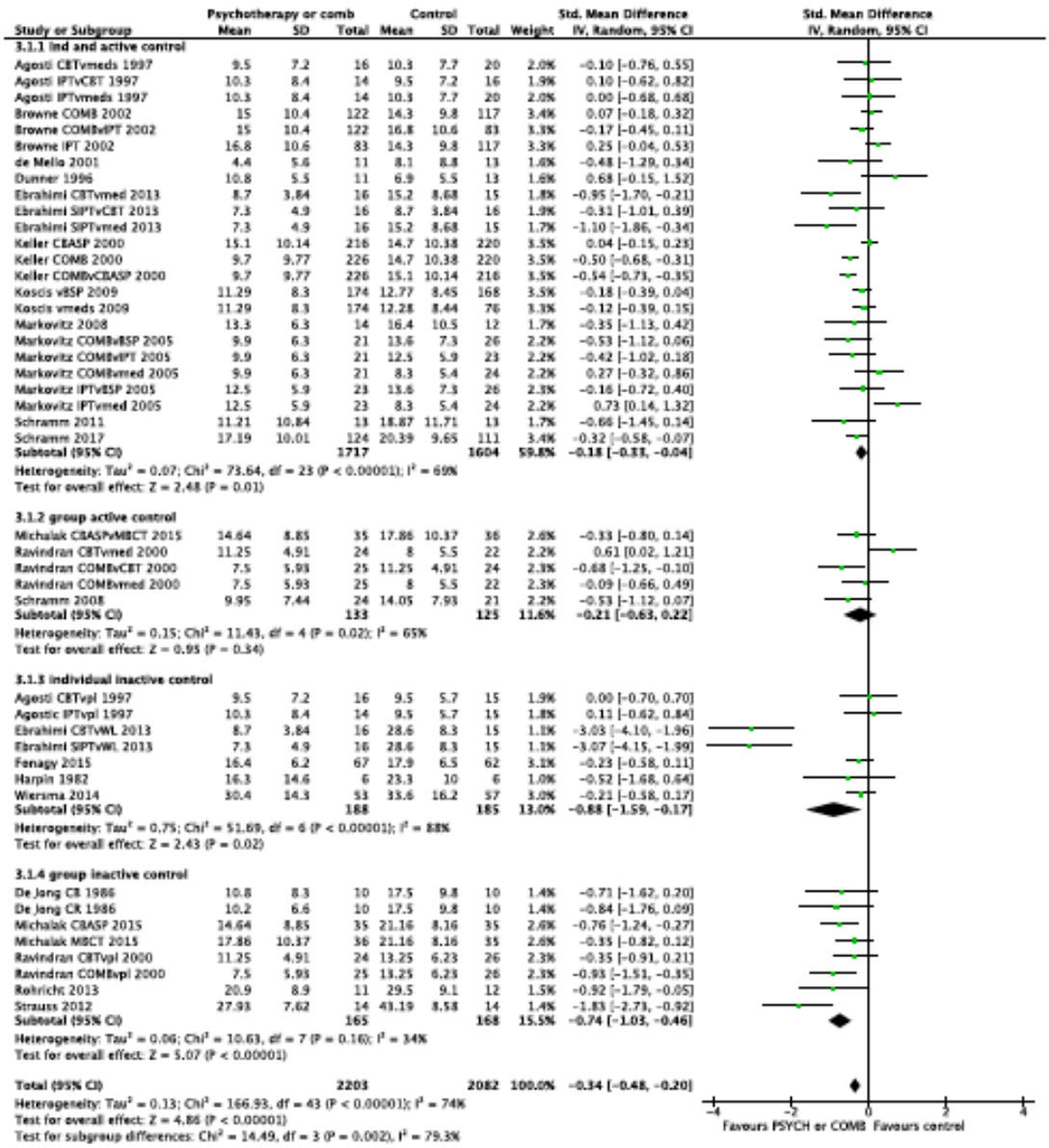
Funnel plot of DYS and chronic

Appendix B. Forest plots from meta-analysis.

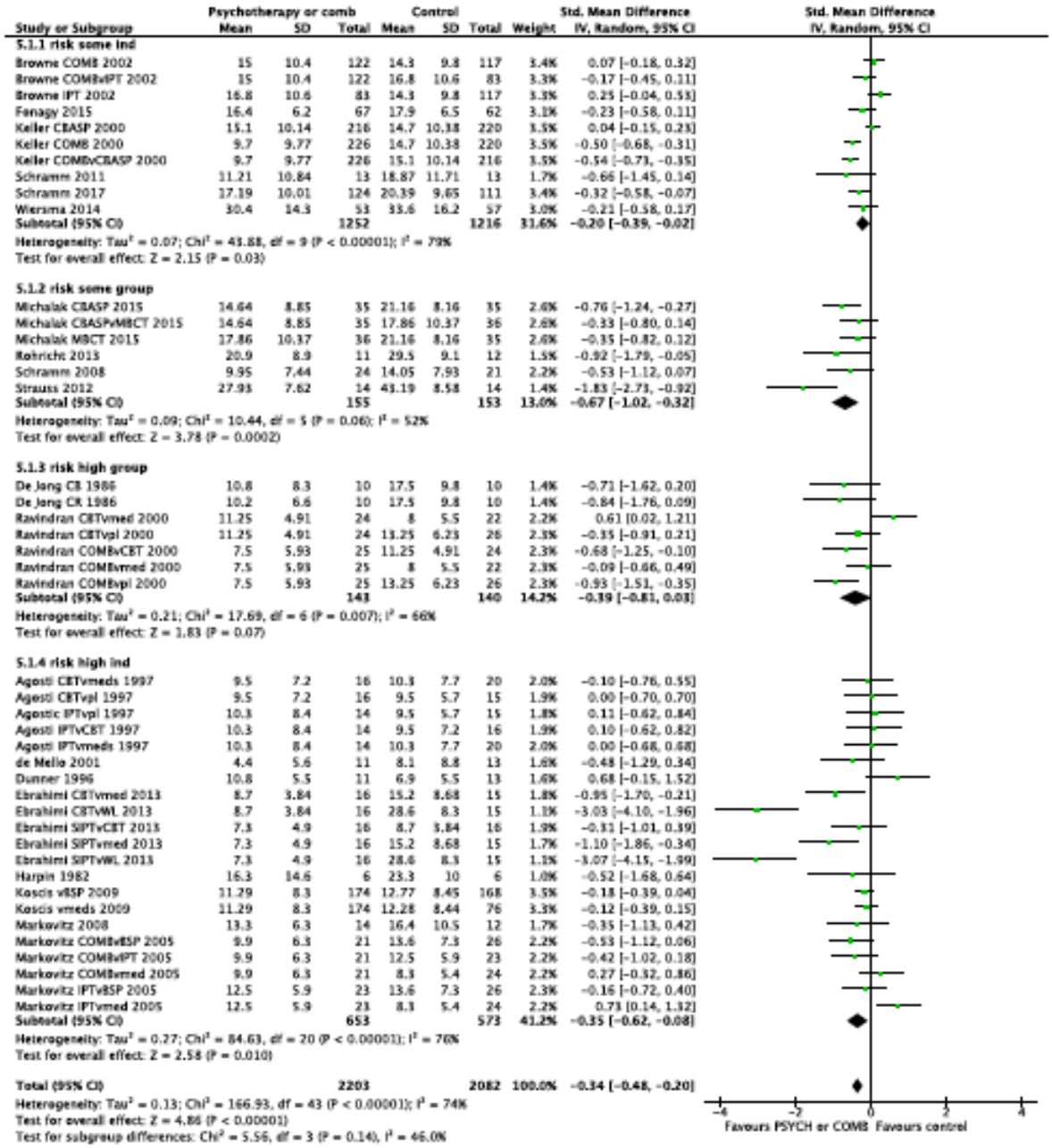
Forest plot of dysthymia and chronic depression (group and individual)



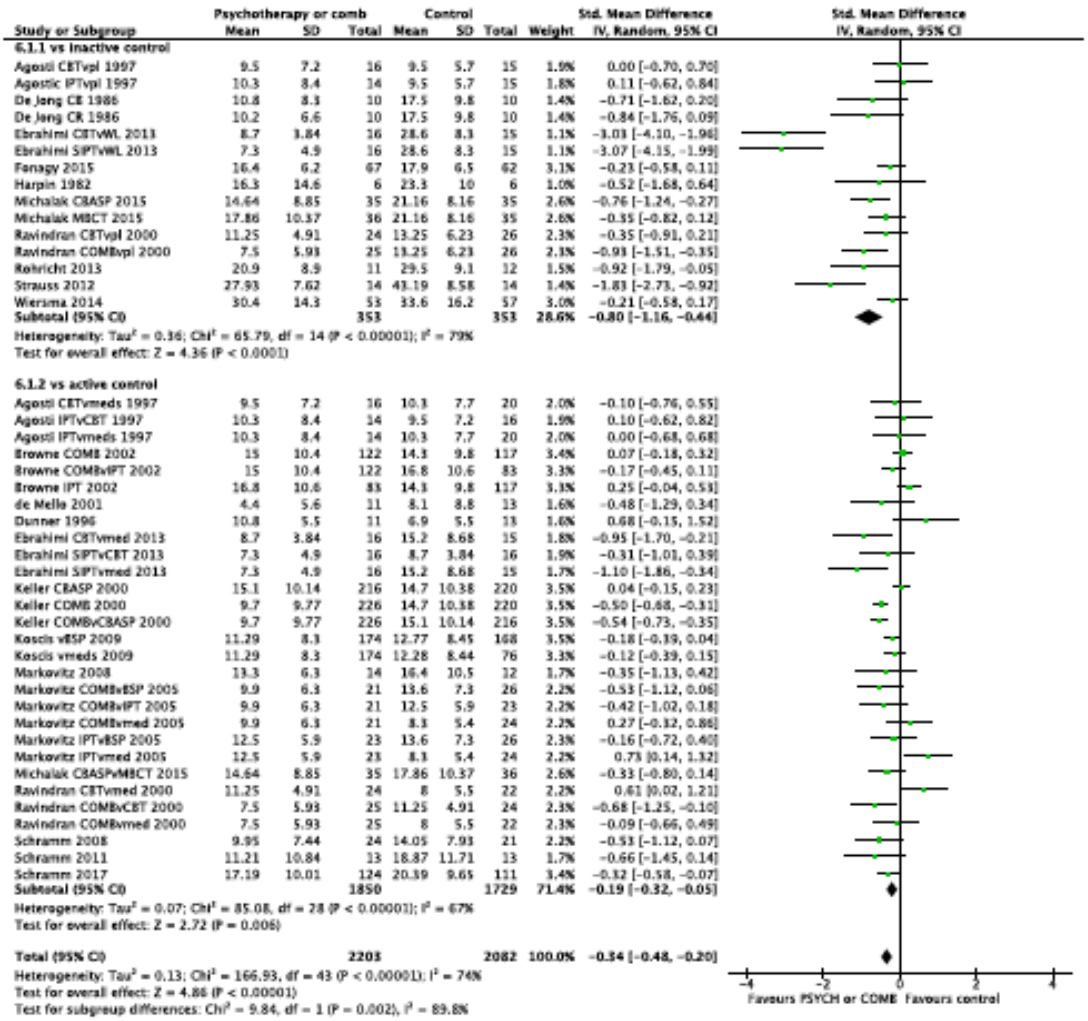
Forest plot of active and inactive controls (group and individual).



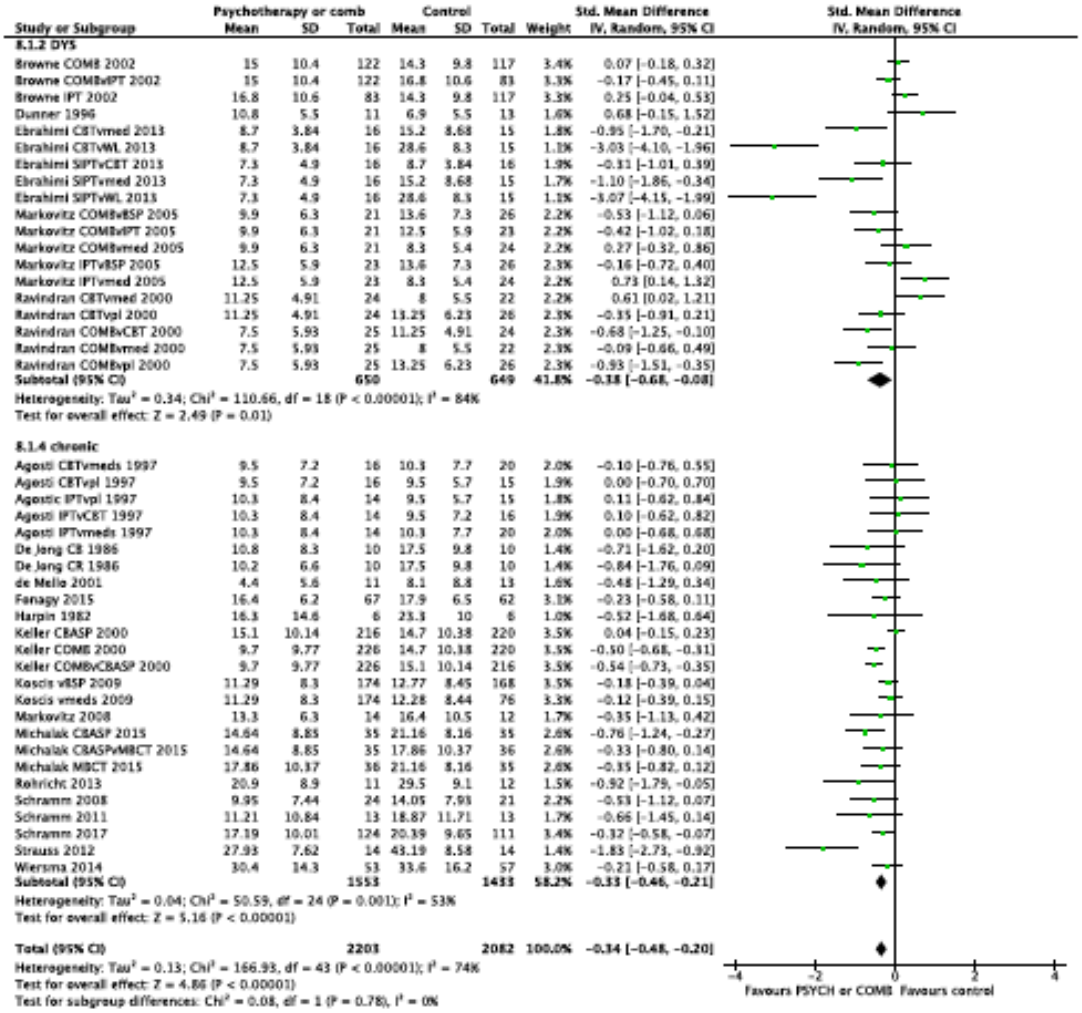
Forest plot of risk of bias.



Forest plot of all inactive and active



Forest plot of all dysthymia and chronic depression.



Appendix C. Interpersonal Circumplex

Interpersonal circles

Autocratic = dominant/controlling

Overly expressive = friendly-dominant/intrusive/needy

Overly nurturant = Friendly/self-sacrificing

Exploitable = Friendly-submissive/overly accommodating

Non-assertive = submissive

Socially avoidant = Hostile-submissive/socially inhibited. Avoidant

Cold = Hostile/distant

Competitive = Hostile-dominant/vindictive/self-centred

connected/disconnected instead of friendly/hostile.

Appendix D. CBASP-G Protocol.

Session	**Date**	**Activity**	**Action**	**Completed**	**FOR NON-DPI** *Did opportunity for DPI arise? Which component?*
1		Timeline and SOH	-PHQ -Check that CBASP manual has been received -Check reaction to manual	Yes / No Yes / No Yes / No	Yes / No **If yes, circle:** 1. IDE 2. CPR 3. Modelling Empathy & Intimacy
2		Timeline and SOH	-PHQ -Timeline completed -SOH completed -PQ-SA (see instructions)(Patient inserts in sealed envelope and therapists puts envelope in file) -After Session 2 therapist completes IMI to be shared in Session 3	Yes / No Yes / No Yes / No Yes / No	Yes / No **If yes, circle:** 1. IDE 2. CPR 3. Modelling Empathy & Intimacy

				Yes / No	
3		Complete Transference Hypothesis, Impact Message Inventory (IMI), Working Alliance (1)	-PHQ -Share IMI (1) -Working Alliance Inventory (Patient and Therapist) completed at end of session	Yes / No Yes / No Yes / No	Yes / No **If yes, circle:** 1. IDE 2. CPR 3. Modelling Empathy & Intimacy
4		IMI	-PHQ -PQ-IDE(1) (see instructions)(Patient inserts in sealed envelope and therapist puts envelope in file) -Letter to referral source	Yes / No Yes / No Yes / No	Yes / No **If yes, circle:** 1. IDE 2. CPR 3. Modelling Empathy & Intimacy
5		Situational Analysis (SA) and/or Interpersonal Discrimination Exercise (IDE)*	-PHQ -SA completed -PPRF completed	Yes / No Yes / No Yes / No	Yes / No **If yes, circle:** 1. IDE

					2. CPR 3. Modelling Empathy & Intimacy
6		SA and/or IDE(DPI)*	-PHQ -SA completed -PPRF completed -PQ-SA(2) (Patient inserts in sealed envelope and therapist puts envelope in file)	Yes / No Yes / No Yes / No Yes / No	Yes / No **If yes, circle:** 1. IDE 2. CPR 3. Modelling Empathy & Intimacy
7		SA and/or IDE(DPI)* Working Alliance (2)	-PHQ -SA completed -PPRF completed --Working Alliance Inventory (Patient and Therapist) completed at end of session	Yes / No Yes / No Yes / No Yes / No	Yes / No **If yes, circle:** 1. IDE 2. CPR 3. Modelling Empathy & Intimacy
Session	**Date**	**Activity**	**Action**	**Completed**	**FOR NON-DPI** *Did opportunity for DPI arise? Which component?*

8		SA and/or IDE (DPI)	-PHQ -PQ-IDE (Patient Inserts in sealed envelope – goes in file) -SA Completed -PPRF Completed	Yes / No Yes / No Yes / No Yes / No	Yes / No **If yes, circle:** 1. IDE 2. CPR 3. Modelling Empathy & Intimacy
9		SA and/or IDE (DPI)	-PHQ -SA Completed -PPRF Completed	Yes / No Yes / No Yes / No	Yes / No **If yes, circle:** 1. IDE 2. CPR 3. Modelling Empathy & Intimacy
10		SA and/or IDE (DPI)	-PHQ -PQ-SA (3) (Patient inserts in a sealed envelope which goes in file) --SA Completed -PPRF Completed	Yes / No Yes / No	Yes / No **If yes, circle:** 1. IDE 2. CPR

				Yes / No Yes / No	3. Modelling Empathy & Intimacy
11		SA and/or IDE (DPI)	-PHQ --SA Completed -PPRF Completed	Yes / No Yes / No Yes / No	Yes / No **If yes, circle:** 1. IDE 2. CPR 3. Modelling Empathy & Intimacy
12		SA and/or IDE (DPI)	-PHQ -PQ-IDE (3)(patient inserts in sealed envelope and therapist puts envelope in file) -SA completed -PPRF completed	Yes / No Yes / No Yes / No Yes / No	Yes / No **If yes, circle:** 1. IDE 2. CPR 3. Modelling Empathy & Intimacy

13		SA and/or IDE(DPI)* Working Alliance (3)	-PHQ -SA completed -PPRF completed -Working Alliance Inventory (Patient and Therapist) completed at end of session	Yes / No Yes / No Yes / No Yes / No	Yes / No **If yes, circle:** 1. IDE 2. CPR 3. Modelling Empathy & Intimacy
14		SA and/or IDE(DPI)*	-PHQ -PQ-SA (4)(patient inserts in sealed envelope and therapist puts envelope in file) -SA completed -PPRF completed	Yes / No Yes / No Yes / No Yes / No	Yes / No **If yes, circle:** 1. IDE 2. CPR 3. Modelling Empathy & Intimacy

Session	**Date**	**Activity**	**Action**	**Completed**	**FOR NON-DPI** *Did opportunity for DPI arise? Which component?*
15		SA and/or IDE (DPI)	-PHQ -SA Completed -PPRF Completed	Yes / No Yes / No Yes / No	Yes / No **If yes, circle:** 1. IDE 2. CPR 3. Modelling Empathy & Intimacy
16		SA and/or IDE (DPI)	-PHQ -PQ-IDE(4)(patient inserts in sealed envelope and therapist puts envelope in file) -SA Completed -PPRF Completed	Yes / No Yes / No Yes / No Yes / No	Yes / No **If yes, circle:** 1. IDE 2. CPR 3. Modelling Empathy & Intimacy
17		SA and/or IDE (DPI)	-PHQ	Yes / No	Yes / No

			--SA Completed -PPRF Completed	Yes / No Yes / No	**If yes, circle:** 1. IDE 2. CPR 3. Modelling Empathy & Intimacy
18		SA and/or IDE (DPI)	-PHQ -PQ-SA(5)(patient inserts in sealed envelope and therapist puts in file) --SA Completed -PPRF Completed	Yes / No Yes / No Yes / No Yes / No	Yes / No **If yes, circle:** 1. IDE 2. CPR 3. Modelling Empathy & Intimacy
19		SA and/or IDE (DPI) Working Alliance (4)	-PHQ -IMI(2) – therapist prepares to be shared in S20 -SA completed -PPRF completed -Working Alliance Inventory (Patient and	Yes / No Yes / No Yes / No Yes / No	Yes / No **If yes, circle:** 1. IDE 2. CPR 3. Modelling Empathy & Intimacy

			Therapist) completed at end of session	Yes / No	
20		SA and/or IDE(DPI)* IMI (2) shared with patient	-PHQ -PQ-IDE(5)(patients inserts in a sealed envelope and therapist puts in file)	Yes / No Yes / No	Yes / No **If yes, circle:** 1. IDE 2. CPR 3. Modelling Empathy & Intimacy

Appendix E. Ethical approval from Edinburgh University.

ISSUES ARISING FROM THE PROPOSAL

Reviewer Comments 8.3.21

There seems to be inconsistent data in the application and granted by caldicott. In the application abov mention SMID also lots of clinical measures.

The caldicott approval states gender, age and CHI numbers. Is it through the CHI numbers that you will clinical measures and SMID? Please clarify.

The applicant should respond to these comments in section below.

Signature: *Position: Ethics and Integrity Lead*
Date: 8.3.21

APPLICANT'S RESPONSE (If required)

The age will be provided from the CHI numbers before anonymisation, so in effect I will not be accessir will be done by someone in the service. The gender and SIMD will be provided to me as per the Caldicot the anonymised form. As stated above Q 43. "Basic demographic information (CHI, age, gender, SIMD)". measures are non-identifiable routinely collected.

Signature:

Date: 09/03/21

CONCLUSION TO ETHICAL REVIEW (if required)

The applicant's response to our request for further clarification or amendments has now satisfied the re for ethical practice and the application has therefore been approved.

Signature:
Position: Lead in Ethics and Integrity/Lecturer in Applied Psychology

Date: 19.3.21

Appendix F. Caldicott ethical approval letter.

Lothian NHS Board

Waverley Gate
2-4 Waterloo Place
Edinburgh
EH1 3EG
Telephone 0131 465 5452

NHS Lothian

Ms Lisa Thompson
Trainee Clinical Psychologist
Lothian Older Peoples Psychology Service
Royal Edinburgh Hospital
Morningside Terrace
Edinburgh EH10 5HF

Date 17 February 2021
Your Ref
Our Ref CG/DF/20194

Enquiries to Caldicott Office
Extension 35452
Direct Line 0131 465 5452
Email Caldicott.Guardian@nhslothian.scot.nhs.uk

Dear Ms Thompson

CALDICOTT APPLICATION 20194

Thank you for the information supplied

Request received from	Ms Lisa Thompson
Summary of proposal	Evaluating the effectiveness and change processes in persistently depressed recipients of group CBASP in an outpatient setting
Patient identifiable information requested	CHI, Age, Gender
Approved	Yes
Advice	

Yours sincerely

Miss Tracey Gillies
Executive Medical Director

Our Values Into Action

disability confident EMPLOYER

CARER POSITIVE Employer in Scotland EXEMPLARY

Headquarters
Waverley Gate
2-4 Waterloo Place
Edinburgh EH1 3EG

Interim Chair Esther Roberton
Chief Executive Calum Campbell
Lothian NHS Board is the common name of Lothian Health Board